Volume 16; Issue No.9; January 2017

Price: ₹ 30 only

AOGD BULLETIN

Women's Health to New Horizons

Theme: Infertility

AOGD SECRETARIAT

1st Floor, PNW I Ward, Maternity Block, Department of Obstetrics and Gynecology
Maulana Azad Medical College & Lok Nayak Hospital, New Delhi-110 002, India
Email: info@aogd.org, aogd@aogd.org; Website: www.aogd.org

AOGD BULLETIN
Volume 16-9, January 2017

Contents

Publisher/Printer/Editor
Dr Sangeeta Gupta on behalf of Association of Obstetricians & Gynecologists of Delhi.

Printed at
Process & Spot C-112/3, Naraina Industrial Area, Phase-1, New Delhi 110 028

Published from
1st Floor, PNW I Ward, Maternity Block, Department of Obstetrics & Gynaecology
Maulana Azad Medical College & Lok Nayak Hospital, New Delhi-110 002, India

Editor
Dr Sangeeta Gupta
Ph. No. 011-23235823; Email: info@aogd.org ; aogd@aogd.org

Total number of pages = 48

AOGD Office-Bearers

Dr Sudha Prasad
President

Dr Reva Tripathi
Advisor

Dr Anjali Tempe
Vice President

Dr Ashok Kumar
Hon. Secretary

Dr Renu Tanwar
Treasurer

Dr Poonam Sachdeva

Dr Poonam Kashyap

Dr Niharika Dhiman

Joint Secretaries

Dr Chetna A Sethi

Dr Preeti Singh

Co Treasurers

Editorial Board

Dr Sangeeta Gupta
Editor

Dr Pushpa Mishra
Web Editor

Dr Krishna Agarwal

Dr Nilanchali Singh

Co-Editors

Dr Bidhisha Singha

Dr Shakun Tyagi

Co-Web Editors

Committees

Dr Y M Mala

Dr Deepti Goswami

Dr Latika Sahu

Monthly Meeting Committee Members

Dr Gauri Gandhi

Dr Madhavi M Gupta

Scientific Committee Members

Dr Devender Kumar

Dr Rachna Sharma

Publicity Committee Members

Dr Asmita M Rathore

Dr Sangeeta Bhasin

Coordinator of Sub-Committee Members

Message from the President

Dear friends

Wishing all of you a very happy New Year!

On the New Year, we look back on all the warm memories and feel proud of our achievements.

From the day we arrived on the planet, it was depicted evidently that the human race was meant to maintain the essence of mankind collectively, rather than setting ourselves apart. Life is represented as a circle because it is a constant loop. There is a spiritual element to the circle, however, in the idea that the end of one existence is not necessarily the end of life altogether.

Today's society has been developing quickly, social media are popular, and more international inventions make everybody over the entire world come closer together. The tendency of globalization is certain. Though this has brought many benefits, stress is a common problem in modern life.

Stress is a basic thing of everyday life and there is no way to escape. The solution to all is a healthy lifestyle. It is a daily package of measures, which consists of a proper balanced diet, exercising, avoiding harmful habits, positive and balanced view of the world.

Let us take a pledge to have a healthy conduct in our daily activities so the joyful spirit keeps glowing.

I wish the coming year brings more and more opportunities to learn new things and grow into a better person and better professional.

Wish you all a successful and prosperous New Year.

"Health is a state of body. Wellness is a state of being." –J. Stanford

"The natural healing force in each one of us is the greatest force in getting well." –Hippocrates

Dr Sudha Prasad
President
drsprasad@yahoo.com

From the Secretary's Desk

Dear Members,

Namaskar!

Wishing you all a very Happy, Healthy & Prosperous New Year 2017. Let us take AOGD to greater heights in coming years.

In this month of festivities highlighted by Christmas and New Year, it is heartening to have various academic activities by AOGD subcommittees all over Delhi (details are under *events held* in this bulletin).

AOGD & Brahmakumaris have organized a Residential Retreat weekend for AOGD family on 24th -25th December, 2016 at Om Shanti Retreat Centre, Manesar to empower us with various spiritual tools. It was found to be very satisfying experience.

A grand 60th AICOG at Ahmedabad is awaiting all of us in this month. Therefore, next monthly clinical meeting at LHMC has been postponed to 3rd February, 2017.

We do hope for your continued active support and participation in all activities in future also!

Dr Ashok Kumar
Honorary Secretary
M: 9968604346
ash64kr@yahoo.com
info@aogd.org
aogd@aogd.org

From the Editor's Pen

Dear friends

Wishing a very happy New Year to all of you.Hope you unfold new horizons, fulfill new wishes, harbor new hopes and rediscover the strength within you to bring in positive changes with the unfolding of the New Year.

Our first issue of the year is dedicated to Infertility. There have been enormous advances in the field of infertility and ART in past few years, yet, we still have many challenges and various issues to address. Management of poor responders in ART cycles remains one of the greatest challenge that infertility specialists all over the world continue to face, and, despite all the research, it remains an enigma.Conservatives estimates show that more than 25,000 children are now being born through surrogates in India every year. There has been lot of discussion and debate over the laws and rights pertaining to surrogacy in India, this has been dealt in detail. Tubal factor infertility accounts for nearly 25-35% of female factor infertility. As we see the improvement and advances in assisted reproduction, many factors need to be taken into consideration while counseling the patients for corrective surgery of ART.

Also, we have an upcoming CME on 'Infertility and Assisted Reproduction'at Maulana Azad Medical College, which is going to be a great academic feast for all of you.

"What was not started today is never finished tomorrow. " –Johann Wolfgang von Goethe

Dr Sangeeta Gupta
Editor
drsangeetamamc@gmail.com

CHANGE IN DATE

Monthly Clinical Meeting

Monthly Clinical Meeting will be held at Lady Harding Medical College & SSK Hospital, New Delhi on **3rd February, 2017** at 4:00pm.

Managing Poor Responders

Sudha Prasad[1], Aishwarya Kapoor[2], Soumya Prasad[2]
[1]Director Professor, [2]Senior Resident, Maulana Azad Medical College, New Delhi

In the field of assisted reproductive technologies great advances have been made in recent years in terms of clinical knowledge and technological development. One of the fundamental steps to reach the success is still related to the number of oocytes obtained after stimulation with gonadotropins in combination with GnRH analogues. In patients defined "poor responders," the limited number of oocytes retrieved remains the main problem in optimizing the live birth rates. In fact, as a result of a lower number of oocytes retrieved, there are fewer embryos to select and transfer and subsequently these patients have lower pregnancy rates per transfer and lower cumulative pregnancy rates per started cycle compared with normal responders. Although the concept of poor ovarian response was introduced over three decades ago, we had not had a common definition of poor responder patients until 2011. The incidence of poor ovarian responders among infertile women has been estimated at 9–24% but according to recent reviews, it seems to have slightly increased.[1]

Etiopathogenesis

There is a physiological decline of the "follicular heritage" in every woman over time with a marked increase in the rate of follicular disappearance from age 37 to 38 years onwards. From this moment, the time to the menopause takes about 10–13 years. In poor responders the mechanism of ovarian insufficiency is prematurely determined and not fully understood. Some causes of decrease in ovarian reserve have been identified: [2,3]

1. ovarian surgery especially in case of endometrioma
2. genetic defects
3. chemotherapy, radiotherapy
4. autoimmune disorders
5. single ovary,
6. chronic smoking
7. unexplained infertility

Moreover, new risk factors of low ovarian response have been proposed:

1. diabetes mellitus Type I[4]
2. transfusion-dependent B-thalassemia[5]
3. uterine artery embolization for the treatment of uterine leiomyoma[6]

However, in most cases the mechanism involved in follicular depletion is still not clear.

Predicting ovarian response

Predicting ovarian response before starting hormonal stimulation is the only way to administer an efficient and safe treatment. The most important predictors of the ovarian response to hormonal stimulation are age, biochemical parameters (basal FSH levels in the early follicular phase, serum antimullerian hormone [AMH]), and morphological characteristics (antral follicular count [AFC] and ovarian volume).[7]

Age: Although ovarian reserve declines with age[8], it does not represent an optimal predictor of ovarian response.

Serum FSH: Basal serum FSH has been considered for many years as the most important and reliable marker to predict the ovarian response to stimulation in IVF/ICSI cycles. Basal serum FSH concentrations begin to rise on average a decade or more before menopause. This is caused by the reduction of the negative feedback of the FSH-modulating proteins from the ovary, mainly inhibin-A and inhibin-B secondary to the reduction of early antral follicles. More recently it has been demonstrated that it is a good predictor only at very high threshold levels (>FSH 12mIU/mL) predicting a much compromised ovarian reserve.

Serum AMH: AMH is produced from preantral follicles and small antral follicles up to 7-8 mm. It inhibits FSH mediated granulosa cell proliferation, follicular growth, and aromatase activity. AMH provides a quantitative evaluation of the amount of follicles that cannot be assessed by AFC. For this reason AMH level has a very low inter- and intracycle variability remaining stable during menstrual cycles but some factors like smoking and current oral contraceptive pills can determine variability. A recent meta-analysis has confirmed AMH as an excellent predictor of poor ovarian response to ovarian stimulation although the ideal test is the response of the ovaries to ovarian stimulation itself. However, the same meta-analysis underlines that AMH and AFC, alone or in combination, did not improve the

prediction of ongoing pregnancy rate, with the age of the woman being the most important factor related to live birth rates.

BMI: Obese poor responders could have a lower pregnancy rate.[8]

Definition of Poor Ovarian Response: The "Bologna Criteria"

Before 2011, a large variety of definitions for poor ovarian response have been published in the literature: the number of mature follicles on the day of human chorionic gonadotropin (hCG) administration (<2 to <5), the number of oocytes retrieved (<4 to <6), the serum estradiol concentrations (<100 pg/mL on day 5 of stimulation or <300 to <600 pg/mL on the day of hCG), or the total gonadotropin dose used and/or the daily stimulation dose and/or prolonged duration of gonadotropin stimulation.

In 2011, a panel of experts in reproductive medicine gathered together in an ESHRE Campus on poor responders held in Bologna with the aim to find a common and universal definition of poor ovarian response. The Bologna ESHRE criteria[9] represent the first real attempt by the scientific community to unify the many definitions proposed to identify poor responder patients by establishing a definite point from which to begin and how to find therapeutic strategies. It was concluded that "poor ovarian responders" should be considered patients having *at least two of the following criteria:*

1. A previous episode of poor ovarian response (≤3 oocytes) with a standard dose of medication.
2. An abnormal ovarian reserve with AFC <5–7 follicles or AMH <0.5–1.1 ng/mL.
3. Women above 40 years of age or presenting other risk factors for poor response such as previous ovarian surgery, genetic defects, chemotherapy, radiotherapy, and autoimmune disorders.

To identify poor responders among women over the age of 40, it is however sufficient to document a reduced ovarian reserve, in the absence of ovarian stimulation.

Management strategies: Is There an Ideal Protocol?

Although many protocols with different doses and types of gonadotropins have been proposed in the literature, to date there is no really efficient treatment that could solve the problem of poor ovarian response and the current question is still which is the ideal protocol for patients defined as *"poor responders".*

Gonadotropins

When the standard dose of gonadotropins (225–300 IU) fails to induce a proper multifollicular growth, the obvious clinical approach is to increase the dose. High doses of gonadotropins have been thus used for poor responder patients. In the literature conflicting data are however reported on the outcomes of this approach: some but not all authors in prospective and retrospective studies report enhanced ovarian response and/or better pregnancy rates with the higher starting dose of gonadotropins up to 450 IU. More recent studies show that gonadotropin of 600 IU/d does not improve outcome of IVF cycles compared with 450 IU/d in women at risk of poor ovarian response.[10] It is today clear that these patients have a reduced ovarian reserve; the recruitable follicles are fewer and the gonadotropins, independently of the dosage administered, can only support the cohort of follicles receptive to stimulation without manufacturing follicles de novo.

GnRH Analogues

In the normal responder women, the standard long agonist protocol is used. However this protocol may have a detrimental effect in poor responders because of excessive ovarian suppression that could lead to a reduced or absent follicular response. For this reason, in patients with poor ovarian reserve the options could be:

1. To decrease the length of suppression by decreasing the duration of GnRH agonist use (short and ultrashort, mini- and microdose flareup regimens).
2. To lower or to stop (after pituitary suppression) the dose of GnRH agonists initiated during the luteal phase.
3. To use the GnRH antagonists in combination with gonadotropins to prevent premature LH rise during the mid-late follicular phase.

Although short and ultrashort flareup regimens are widely used in poor responder patients for more than 20 years, all published studies, including a recent meta-analysis were unable to demonstrate clearly any significant beneficial effect on the clinical outcome in this group of patients.[11]

The rationale to lower or to stop (after pituitary suppression) the dose of GnRH agonists initiated during the luteal phase is to obtain a reduction of

the inhibitory direct effect of the GnRH agonist on the ovaries. There have been conflicting results of various studies and as per a recent meta-analysis, no statistically significant difference was present in clinical pregnancy rates per cycle randomized between the "GnRH agonist stopped protocol" and the standard agonist protocol.[11]

GnRH Antagonist

The use of GnRH antagonist was introduced in the clinical practice about 15 years ago. The most important advantages of the use of GnRH antagonist in combination with gonadotropins are decreased number of days of stimulation and of the amount of gonadotropin administered and significant reduction of ovarian hyperstimulation syndrome (OHSS).

Furthermore, GnRH antagonists are not administered during the stage of follicular recruitment and thus suppression of endogenous gonadotropins secretion is not present at that time in contrast to GnRH agonists being a possible advantage during ovarian stimulation in this group of patients. For these reasons, several authors suggested the use of GnRH antagonists in combination with gonadotropins as a suitable protocol for poor responders. In fact, GnRH antagonists in the mid-late follicular phase during ovarian stimulation prevent the premature LH surge while not causing suppression in the early follicular phase, obtaining more natural follicular recruitment without any inhibitory effect possibly induced by the GnRH agonist.

However, a metaanalysis of randomized controlled trials demonstrated that stimulation protocols where GnRH antagonist is used in combination with gonadotropins result in similar pregnancy rates compared with long agonist or short flareup regimens.[12]

Although there is not a stimulation protocol that significantly improves the clinical outcome in poor responder patients and that can be considered as a standard of medical care practice, the use of GnRH antagonist regimens could have some advantages over the GnRH agonist protocols.

1. It is possible to assess the ovarian reserve by ultrasound on days 2-3 of the cycle in which COH is planned and decide whether to initiate gonadotropins in the cycle where the probability of a favorable response is optimal. In fact, patients with a mean follicle count of <5 follicles have significant cycle-to-cycle variability in antral follicle count from −2 to +5 to −3 to +7.
2. With use of GnRH antagonist to prevent premature LH rise we can utilize a new gonadotropin, a hybrid molecule with a prolonged half-life (corifollitropin alfa) that supports the cohort of follicle receptive to stimulation for seven days.

Corifollitropin Alfa

The use of these long acting gonadotropins could exploit fully the reduced ovarian reserve by the rapid increase in the serum FSH concentration that would result in a significantly higher exposure of the small antral follicles to constant high levels of FSH during the early follicular phase. The peculiar pharmacokinetic of this molecule seems to be able to exploit fully the reduced ovarian reserve. Higher pregnancy rates were reported in a retrospective pilot study in young (<40 years) poor responder patients following a combination of corifollitropin alfa with hp-HMG in a GnRH antagonist protocol.[13] Moreover, the reduction of the number of daily subcutaneous injections of gonadotropins could reduce the physical and psychological burdens for these patients. A recent randomized trial failed to demonstrate a significant benefit, however sample size was small and further studies are needed to evaluate the utility in poor responders.[14]

Alternative Approaches

Several alternative approaches have been proposed with the aim of strengthening the effect of exogenous gonadotropins.

Addition of Estradiol in the Luteal Phase: It has been found that the addition of estradiol in the luteal phase with or without the simultaneous use of GnRH antagonist decreases the risk of cycle cancellation and increases the chance of clinical pregnancy in poor responder patients. The biological rationale might be that luteal estradiol priming could improve synchronization of the pool of follicles available to controlled ovarian stimulation.[15] However, further randomized trials are needed before suggesting the addition of estradiol in the luteal phase.

Addition of Recombinant LH: Some authors suggested the addition of recombinant LH during gonadotropin stimulation in poor responder patients. However, two metaanalysis showed that the addition of recombinant LH does not increase the number of oocyte retrieved, the total dose of FSH, the cancellation rates, and the ongoing pregnancy rates in poor responder patients. On the other hand, in a very recent meta-analysis of 40 randomized controlled studies, significantly more oocytes were retrieved and significantly higher clinical pregnancy rates were observed with rhFSH plus

r-hLH versus r-hFSH treatment in poor responders, suggesting that there is a relative increase in the clinical pregnancy rates of 30% in poor responders and that the addition of r-hLH to r-hFSH may be beneficial for women with poor ovarian response.[16]

Addition of Growth Hormone: It has been suggested that the use of growth hormone (GH) might modulate the action of FSH on granulosa cells by upregulating the local synthesis of insulin-like growth factor-I (IGF-I). The IGF-I amplifies the effect of FSH at the level of both granulosa and theca cells. Two recent meta-analyses of 6 randomized trials (128 patients in total) suggested that addition of GH significantly increased the probability of live birth in poor responders. Regarding GH administration, frequency and dosage varied markedly among the eligible studies. However, due to the small number of the patients and the heterogeneity of the frequency and dosage of GH administered amongst the studies, the fact that the addition of GH during ovarian stimulation enhances the probability of pregnancy needs to be evaluated in further properly designed trials to prove or disprove this finding.[17]

Addition of Androgens: Androgens, produced primarily by theca cells, play a critical role for an adequate follicular steroidogenesis and for a correct early follicular and granulosa cell development. The substrate for the aromatase activity of the granulosa cells, which converts the androgens to estrogens. Moreover, androgens may increase FSH receptor expression in granulosa cells amplifying the effects of FSH and thus potentially enhance responsiveness of ovaries to FSH. Furthermore, inadequate levels of endogenous androgens are associated with decreased ovarian sensitivity to FSH and low pregnancy rates after IVF.

Based on these observations Casson et al.[18] first suggested that the oral administration of dehydroepiandrosterone (DHEA) before ovarian stimulation with gonadotropin could improve the response in poor responder patients. A recent meta-analysis of four randomized controlled trials of adjuvant androgens (DHEA and testosterone) in poor responder patients showed a significantly higher ongoing pregnancy rate in the androgen supplementation group.[19] However, the included studies were too small and presented clinical and methodological heterogeneity to be conclusive and to warrant an immediate change in practice.

Addition of Aspirin: Increased intra ovarian vascularity has been linked to improved delivery of gonadotropic hormones or other growth factors required for folliculogenesis On the other hand, impaired ovarian blood flow could contribute to poor ovarian response. Based on this rationale, by enhancing ovarian vascularization with vasoactive substances such as aspirin, the ovarian response could theoretically improve. However, the evidence supporting the effect of a low dose of aspirin in women undergoing IVF is poor and controversial. Prospective randomized trials demonstrated that adjuvant therapy with aspirin and prednisolone did not improve uterine blood flow, implantation, and pregnancy rates.[20]

Natural Cycles IVF: Natural cycles IVF with or without minimal stimulation can be considered as an easy and cheap approach in the management of poor responders. In fact, some authors suggested that natural cycles IVF was a valid option for poor responder patients because it has the same chance in terms of pregnancy and implantation rates.[21]

Oocyte Cryopreservation: Oocyte vitrification has resulted in the breakthrough in ART technologies. Different strategies are applicable for poor responder involving oocyte cryopreservation. Some authors have recently suggested obtaining a large cohort of oocytes in these patients by accumulating vitrified oocytes over several stimulation cycles creating a similar situation as in normal responder patients. According to the results presented in the study, it could be possible to obtain higher live birth rate per patient treated and potentially to reduce the dropout.[22] Moreover, oocyte cryopreservation can also be used to preserve the fertility of all those women at risk to lose their ovarian potential over the time.

Freeze all: Various studies suggest improved pregnancy outcomes from blastocyst culture and cryopreservation in poor responders.[23]

Aromatase inhibitors: One of the recent studies have suggested that letrozole incorporated in GnRH antagonist protocol may be more effective resulting in comparable pregnancy outcomes with shorter duration and smaller dose of rhFSH, when compared with the standard GnRH antagonist protocol.[24]

ICSI: Conventional IVF and ICSI are associated with similar reproductive outcomes in poor responder patients with a single oocyte retrieved.[25]

Myoinosotol (MI): Some recent studies suggest that MI therapy in poor responders results in an increased of the number of oocytes and increase in the gonadotropin Ovarian Sensitivity Index (OSI), suggesting a MI role in improving ovarian response to gonadotropins. Therefore MI may be helpful in "poor responders" undergoing IVF cycles.[26]

Conclusion

Despite the two decades of trying, there is still no consensus on what is best for poor responders. No single treatment can be recommended over another, as the evidence for all of them is insufficient A very promising stimulation protocol is in fact represented by the combination of corifollitropin alfa with HP-HMG in a GnRH antagonist regimen. However, prospective studies are necessary to confirm the possible benefit of this approach. It is obvious that interventions used in poor responders require properly designed large randomized studies, because until now there is no evidence-based treatment for that particular group of patients.[27]

References

1. Polyzos NP, Devroey P. A systematic review of randomized trials for the treatment of poor ovarian responders: is there any light at the end of the tunnel? Fertil Steril 2011; 96:1058-61.
2. Streuli I, de Ziegler D, Gayet V, Santulli P, Bijaoui G, de Mouzon J, Chapron C. In women with endometriosis anti-Müllerian hormone levels are decreased only in those with previous endometrioma surgery. Hum Reprod. 2012; 27:3294-303.
3. Raffi F, Metwally M, Amer S. The impact of excision of ovarian endometrioma on ovarian reserve: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2012; 97:3146-54.
4. Soto N, Iñiguez G, López P, Larenas G, Mujica V, Rey RA, Codner E. Anti-Mullerian hormone and inhibin B levels as markers of premature ovarian aging and transition to menopause in type 1 diabetes mellitus. Hum Reprod. 2009; 24:2838-44.
5. Chang HH, Chen MJ, Lu MY, Chern JP, Lu CY, Yang Y et al. Iron overload is associated with low anti-müllerian hormone in women with transfusion-dependent β-thalassaemia. BJOG. 2011; 118:825-31.
6. Tropeano G, Di Stasi C, Amoroso S, Gualano MR, Bonomo L, Scambia G. Long-term effects of uterine fibroid embolization on ovarian reserve: a prospective cohort study. Fertil Steril. 2010; 94:2296-300.
7. Dólleman M, Faddy MJ, van Disseldorp J, van der Schouw YT, Messow CM, Leader B et al. The relationship between anti-Müllerian hormone in women receiving fertility assessments and age at menopause in subfertile women: evidence from large population studies. J Clin Endocrinol Metab. 2013; 98:1946-53.
8. Vural F, Vural B, Çakıroğlu Y. The Role of Overweight and Obesity in In Vitro Fertilization Outcomes of Poor Ovarian Responders. Biomed Res Int. 2015; 2015:781543.
9. Ferraretti AP, La Marca A, Fauser BC, Tarlatzis B, Nargund G, Gianaroli L. ESHRE consensus on the definition of 'poor response' to ovarian stimulation for in vitro fertilization: the Bologna criteria. Hum Reprod. 2011; 26:1616-24.
10. Lefebvre J, Antaki R, Kadoch IJ, Dean NL, Sylvestre C, Bissonnette F et al. 450 IU versus 600 IU gonadotropin for controlled ovarian stimulation in poor responders: a randomized controlled trial.Fertil Steril. 2015; 104:1419-25.
11. Kyrou D, Kolibianakis EM, Venetis CA, Papanikolaou EG, Bontis J, Tarlatzis BC. How to improve the probability of pregnancy in poor responders undergoing in vitro fertilization: a systematic review and meta-analysis. Fertil Steril 2009; 91:749-66.
12. Pu D, Wu J, Liu J. Comparisons of GnRH antagonist versus GnRH agonist protocol in poor ovarian responders undergoing IVF. Hum Reprod. 2011; 26:2742-9.
13. Polyzos NP, Devos M, Humaidan P, Stoop D, Ortega-Hrepich C, Devroey P. Corifollitropin alfa followed by rFSH in a GnRH antagonist protocol for poor ovarian responder patients: an observational pilot study. Fertil Steril. 2013; 99:422-6.
14. Kolibianakis EM, Venetis CA, Bosdou JK, Zepiridis L, Chatzimeletiou K, Makedos A et al. Corifollitropin alfa compared with follitropin beta in poor responders undergoing ICSI: a randomized controlled trial. Hum Reprod. 2015; 30:432-40.
15. Reynolds KA, Omurtag KR, Jimenez PT, Rhee JS, Tuuli MG, Jungheim ES. Cycle cancellation and pregnancy after luteal estradiol priming in women defined as poor responders: a systematic review and meta-analysis. Hum Reprod 2013; 28:2981-9.
16. Lehert P, Kolibianakis EM, Venetis CA, Schertz J, Saunders H, Arriagada P et al. Recombinant human follicle-stimulating hormone (r-hFSH) plus recombinant luteinizing hormone versus r-hFSH alone for ovarian stimulation during assisted reproductive technology: systematic review and meta-analysis. Reprod Biol Endocrinol. 2014; 20; 12:17.
17. Eftekhar M, Aflatoonian A, Mohammadian F, Eftekhar T. Adjuvant growth hormone therapy in antagonist protocol in poor responders undergoing assisted reproductive technology. Arch Gynecol Obstet. 2013; 287:1017-21.
18. Casson PR, Santoro N, Elkind-Hirsch K, Carson SA, Hornsby PJ, Abraham G at al. Postmenopausal dehydroepiandrosterone administration increases free insulin-like growth factor-I and decreases high-density lipoprotein: a six-month trial. Fertil Steril. 1998; 70:107-10.
19. Sunkara SK, Coomarasamy A. Androgen pretreatment in poor responders undergoing controlled ovarian stimulation and in vitro fertilization treatment. Fertil Steril 2011; 95:e73-4.
20. Frattarelli JL1, McWilliams GD, Hill MJ, Miller KA, Scott RT Jr. Low-dose aspirin use does not improve in vitro fertilization outcomes in poor responders. Fertil Steril 2008; 89:1113-7.
21. Schimberni M, Morgia F, Colabianchi J, Giallonardo A, Piscitelli C, Giannini P et al. Natural-cycle in vitro fertilization in poor responder patients: a survey of 500 consecutive cycles. Fertil Steril. 2009; 92:1297-301.

22. Cobo A, Garrido N, Crespo J, José R, Pellicer A. Accumulation of oocytes: a new strategy for managing low-responder patients. Reprod Biomed Online. 2012; 24: 424-32.
23. Berkkanoglu M, Coetzee K, Bulut H, Ozgur K .Optimal embryo transfer strategy in poor response may include freeze-all. J Assist Reprod Genet. 2016. (Epub ahead of print).
24. Lee KH, Kim CH, Suk HJ, Lee YJ, Kwon SK, Kim SH. The effect of aromatase inhibitor letrozole incorporated in gonadotrophin-releasing hormone antagonist multiple dose protocol in poor responders undergoing in vitro fertilization. Obstet Gynecol Sci. 2014; 57:216-22.
25. Sfontouris IA, Kolibianakis EM, Lainas GT, Navaratnarajah R, Tarlatzis BC, Lainas TG. Live birth rates using conventional in vitro fertilization compared to intracytoplasmic sperm injection in Bologna poor responders with a single oocyte retrieved. J Assist Reprod Genet. 2015; 32:691-7.
26. Caprio F, D'Eufemia MD, Trotta C, Campitiello MR, Ianniello R, Mele D et al. Myo-inositol therapy for poor-responders during IVF: a prospective controlled observational trial. J Ovarian Res. 2015; 12; 8:37.
27. Szymusik I, Marianowski P, Zygula A, Wielgos M. Poor responders in IVF--is there any evidence-based treatment for them? Neuro Endocrinol Lett. 2015; 36:209-13.

AOGD Sub-Committees Chairpersons

S. No.	Sub-Committee Name	Year	Chairperson	Email.id
1.	Adolescent Health	2015-17	Dr Mamta Mittal	drmamtamittal@gmail.com
2.	Breast Cancer Prevention	2016-18	Dr Sunita Malik	svmalik@yahoo.com
3.	Cervical Cancer Awareness and Prevention	2016-18	Dr Mala Srivastava	malasrivastava2001@yahoo.co.in
4.	Endometriosis	2015-17	Dr Ramandeep Kaur	dr.ramandeep@ymail.com
5.	Endoscopy	2015-17	Dr Neema Sharma	drneemasharma@yahoo.com
6.	Fetal Medicine & Genetics	2015-17	Dr Seema Thakur Dr Chanchal Singh	seematranjan@gmail.com chanchalsingh@gmail.com
7.	Infertility	2016-18	Dr K D Nayar	kdnayar@usa.net
8.	Multidisciplinary Patient Management	2016-18	Dr Jyotsna Suri	jyotsnasuri@gmail.com
9.	Oncology	2015-17	Dr Shalini Rajaram	rajaram.shalini@gmail.com
10.	Reproductive Endocrinology	2015-17	Dr Susheela Gupta	drsusheelagupta@gmail.com
11.	Rural Health	2016-18	Dr Achla Batra	achla_batra@yahoo.com
12.	Safe Motherhood	2015-17	Dr Abha Singh	abhasinghlhmc@gmail.com
13.	Urogynaecology	2015-17	Dr Ranjana Sharma	rnj_sharma@yahoo.com

The sub-committee members are requested to intimate activities of the sub-committee to the AOGD secretariat through the chairperson. The form for conducting the activity is available on AOGD website www.aogd.org

The members of AOGD who wish to conduct activities are requested to contact the respective sub-committee chairperson.

Endometrial Scratching: Is it a necessity?

Anjali Tempe[1], Deepali Dhingra[2], Akansha Sahare[3]
[1]Director Professor, [2]Fellow, Reproductive Medicine, [3]Post Graduate, Maulana Azad Medical College, New Delhi

In an era of great advances in reproductive medicine, the pregnancy and live birth rates of in-vitro fertilization (IVF) and intra cytoplasmic sperm injection (ICSI) remains low. Implantation failure remains the most common cause of failure of IVF-ICSI procedure. A dialogue between embryo and endometrium is absolutely essential for a successful implantation. In humans endometrium is most receptive during day 19-23 of menstrual cycle.[1] For a successful implantation to happen, a normal blastocyst should be able to hatch, appose, adhere, penetrate, and finally invade a well-receptive endometrium. A receptive endometrium is regulated by alteration in gene expression of cytokines, growth and transcription factors as well as adhesive molecules.[2] Recently, mechanical injury to endometrium in the form of "scratching" has been shown to improve implantation and successful IVF procedure. Hysteroscopy is another form of mechanical manipulation of endometrium. Because of the difference in timing to induce local injury and different methods to induce injury, there is considerable heterogeneity of studies.

Mechanism of action

Endometrial injury and its effect on implantation were first studied by Barash *et al*. in 2003. There are few probable mechanisms which make scratching of endometrium responsible to improve implantation. It upregulates cytokines, growth factors, interleukins, macrophages, and dendritic cells, all of which improve the cross-talk of embryo and endometrium.[3] Healing which follows after endometrial injury slows down endometrial maturation which occurs in Controlled ovarian hyperstimulation (COS) cycles.

Timing

Endometrial scratching is best performed in a cycle prior to embryo transfer cycle. Many studies reported different timing in relation to menstrual cycle. Performing injury in preceding cycle is more effective as the mechanisms involving beneficial effects of endometrial injury require time.

Procedure

The procedure takes 15-20 minutes and may be a little discomforting to the patient but usually no anaesthetic is required. The procedure is similar to an embryo transfer or cervical smear test. A speculum is gently inserted into the vagina and the cervix is cleaned with sterile gauze. A fine, thin plastic tube (flexible catheter or IUI catheter) is passed through the opening of the cervix into the uterine cavity to gently and superficially scratch the lining of the uterus and the catheter is then taken out at the end of the procedure.

Side effects

Although Endometrial scratch is a very safe procedure, some side effects may follow such as:

- Mild cramping pains during and after the procedure
- Mild bleeding
- Rarely pelvic infection

Literature

Barash *et al*. in 2003[4] demonstrated that endometrial biopsy performed on days 8, 12, 21, and 26 of the menstrual cycle is associated with higher pregnancy rate. Raziel *et al*. in 2007[5] conducted a prospective study on 120 couples with high-order implantation failure of >4 unsuccessful ET of fresh embryos. They performed endometrial biopsy twice on days 21 and 26 of the preceding ovarian stimulation cycle and concluded that implantation rate was significantly higher for patients who had undergone biopsy. However, no statistically significant difference was observed for the ongoing pregnancy and miscarriage rates. Narvekar *et al*. in 2010[6] did a randomized controlled trial (RCT) and concluded that implantation and clinical pregnancy rate was significantly higher in endometrial scratching group when done in non-transfer cycle. Nastri C *et al* in a RCT in 2013, demonstrated that endometrial scratching performed during oral contraceptive pill (OCP) pre-treatment 7–14 days before starting COS, increases the chance clinical pregnancy and live birth.[7]

Conclusion

Endometrial scratching is simple and inexpensive procedure, the benefits of which far outweigh the side effects of pain and infection. With local endometrial

injury there are changes in immune mechanisms and gene expression within the endometrium and these changes take time to prove their beneficial effects, so the concept of doing it in non-transfer cycle. But it comes with a question that whether endometrial scratching should be done in all IVF cycles or patients with recurrent implantation failure. Also other factors like timing of procedure, its relation with hysteroscopy, and single or multiple scratchings needs to be answered.

References

1. H. Achache, A. Tsafrir, D. Prus, R. Reich, A. Revel. Defective endometrial pro staglandin synthesis identified in patients with repeated implantation failure undergoing in vitro fertilization. Fertil Steril, 94 (2010), pp. 1271–1278.
2. Kalma, Y., Granot, I., Gnainsky, Y., Or, Y., Czernobilsky, B., Dekel, N., Barash, A., 2009. Endometrial biopsy-induced gene modulation: first evidence for the expression of bladder-transmembranal uroplakin Ib in human endometrium. Fertil. Steril. 91, 1042–1049.
3. Gnainsky Y, Granot I, Aldo PB, Barash A, Or Y, Schechtman E, et al. Local injury of the endometrium induces an inflammatory response that promotes successful implantation. Fertil Steril. 2010;94:2030–6.
4. Barash A, Dekel N, Fieldust S, Segal I, Schechtman E, Granot I. Local injury to the endometrium doubles the incidence of successful pregnancies in patients undergoing *in vitro* fertilization. Fertil Steril. 2003;79:1317–22.
5. Raziel A, Schachter M, Strassburger D, Bern O, Ron-El R, Friedler S. Favorable influence of local injury to the endometrium in intracytoplasmic sperm injection patients with high-order implantation failure. Fertil Steril. 2007;87:198–201.
6. Narvekar SA, Gupta N, Shetty N, Kottur A, Srinivas M, Rao KA. Does local endometrial injury in the nontransfer cycle improve the IVF-ET outcome in the subsequent cycle in patients with previous unsuccessful IVF?. A randomized controlled pilot study. J Hum Reprod Sci. 2010;3:15–9.
7. Nastri CO, Ferriani RA, Raine-Fenning N, Martins WP. Endometrial scratching performed in the non-transfer cycle and outcome of assisted reproduction: A randomized controlled trial. Ultrasound Obstet Gynecol. 2013; 42:375–82.

Obituary

The sad demise of Dr. Rakesh Sinha on 26th Decemder, 2016, is an unfortunate and shocking news for the entire medical fraternity. Dr Rakesh Sinha, considered a pioneer in the field of endoscopic gynaecology in the country, would have turned 60 on January 11, 2017. He was a great human being, superb orator, a world renowned motivational speaker, author of numerous gynecologic endoscopy books and recently wrote a book on Success published by Harper Collins. A teacher of teachers, a great gyne endoscopist, a Guinness book of World record holder and a multi-talented, versatile person. A fitness freak, fashion icon in himself with a great smile and wow eye contact while speaking to his colleagues and friends. He was our past IAGE President. He was a down to earth human being, help those who required his advise and had no ego issues with anyone. He was an institute by himself. It's a very big loss not only to India but to the world gyne endoscopy fraternity. I am sure all of us have great memories of him. May his soul Rest in Peace!

Tubal Surgeries In Era of ART

Renu Tanwar
Professor, Maulana Azad Medical College, New Delhi

Introduction

Tubal disease accounts for 25%-35% of female factor infertility with more than half the cases are due to salpingitis.[1]

Reconstructive surgery was the only therapeutic option for infertility caused by tubal and peritoneal factors till the mid 1980s. Simultaneously laparoscopic access was explored for tubal reconstruction as it could be performed on day care basis and enabled surgical modification for more complex cases.

The IVF results significantly improved during the 1990s and since than it began to be offered as the primary treatment option for tubal factor infertility. Hence being concerned with this rising trend of IVF, there is a need to determine the optimal treatment methods for these patients and the factors that need to be considered when deciding between surgical repair and IVF

Factors that need to be considered when counselling patients regarding tubal surgery or IVF

- Age
- Ovarian reserve
- Prior Fertility
- Presence of other infertility factors
- Site and extent of tubal disease
- Experience of the surgeon
- Success rate of IVF program
- Cost, patient preference and religious belief

Husband Semen Analysis result may influence the management decision between tubal surgery & IVF

Proximal Tubal Disease

Tubal spasm or transient occlusion by mucus plugs occurs in upto 40% of cases.[2] Laparoscopic guided hysteroscopic cannulation is the choice in these cases and has the advantage of examination of the abdomen & pelvis, gives information of distal tube and underlying disease and also has no radiation exposure. Meta-analysis has shown that in approximately 85% of the tubes, the obstruction is relieved with tubal cannulation and approximately half conceive.[1] Selective salpingography or tubal cannulation under USG guidance can also restore tubal patency but its diagnostic accuracy is inferior.

If the obstruction is not overcome by tubal cannulation with gentle pressure than procedure is terminated and true anatomic occlusion is assumed due to SIN, chronic salpingitis or obstructive fibrosis in 93% of patients.[3] In these cases and in older women and in presence of significant male factor- IVF is preferred to resection and microsurgical tubo-cornual anastomosis.

Microsurgery may be considered for failed tubal cannulation if IVF is not the option for the patient but microsurgery should be attempted by those with appropriate training.

Distal Tubal Disease

It includes hydrosalpinges and fimbrial phimosis and is due to PID or peritonitis of any cause or tubal damage from previous surgery.

Fimbrial phimosis (agglutination of the fimbriae) often coexist with periadnexal adhesions and this necessitates a laparoscopic fimbrioplasty. The reported cumulative intrauterine pregnancy rate range from 40%-48% and ectopic pregnancy rates are 5%-6%.[4]

Intraoperative salpingoscopy enables direct endoscopic evaluation of tubal mucosa which may facilitate a decision to perform conservative salpingoneostomy or on the basis of extensive tubal pathology- salpingectomy in preparation of IVF.[5]

Good prognosis is associated with

– limited flimsy adnexal adhesions

– mildly dilated tube <3cm with thin and pliable walls

– Preservation of mucosal folds

Intrauterine pregnancy rates and ectopic pregnancy rates after neosalpingostomy for mild hydrosalpinges range from 58%-77% and 2% to 8% respectively.[6]

Prognosis is poor in presence of intratubal adhesions, absence of mucosal folds with flattened patches of scarred mucosa.

Salpingostomy is not indicated in rigid, thick walled hydrosalpinges, poor prognosis hydrosalpinges and in women with proximal and distal occlusion.

IVF preferred over salpingostomy for mild

hydrosalpinges in older women and those with male factor or other infertility factors.

Laparoscopic salpingectomy or occlusion should be considered before IVF for women with communicating hydrosalpinges as well as poor prognosis hydrosalpinx and great care is taken not to interfere with ovarian blood supply via the infundibulopelvic fold. Live birth rates achieved with IVF among women with hydrosalpinges is approximately one half that observed in women without hydrosalpinges.[7]

Randomized control trails have found that tubal ligation by mechanical clips was better than using bipolar cautery.[8] Ultrasound guided aspiration of hydrosalpinx at the time of oocyte retrieval has also reported significantly higher clinical pregnancy rate.[9]

Proximal occlusion by essure coil inserts via hysteroscope has also been used but data on IVF success rate is limited.

Surgery for Sterilization Reversal

Microsurgery has its ultimate application in tubo-tubal anastomosis and offers a high chance of tubal patency and fertility in women wishing to conceive after Hulka clip or Filshie and Fallope ring sterilization. In absence of a male factor the major factors that affect outcome are

- Age of the women
- Length of residual fallopian tube
- Site of tubal anastomosis
- Quality of the microsurgical technique

Women with normal ovarian function and who are less than 37 years of age can anticipate a cumulative live birth rate of about 70%, with most pregnancies occurring within 12 months after surgery and an ectopic pregnancy rate as low as 2% [10]

Ideally the reconstructed tube should not be less than 5 cm long. Proper function requires the presence of ampullary-infundibular segment of approximately 3cm and an isthmic segment of 2 cm to enable oocyte capture and retention. Isthmic-Isthmic repair and combined final tubal length yield higher success rate.

Robotic technology has also been used but further studies are needed to evaluate the risk, benefits and cost effectiveness.

Tubal anastomosis should not to be considered

- When final tubal length <4 cm
- Significant tubo-ovarian adhesion or stage III-IV endometriosis
- When there is more than mild male factor

Conclusion

The choice of primary treatment and any subsequent treatment should be dependent on careful investigation of the patient and should be individualized. IVF IS THE THERAPEUTIC OPTION for those with inoperable tubal damage and for those with tubal disease coincident with another infertility factor[11]. Those with tubal factor as the sole cause of infertility and that is amenable to surgery, successful surgery will offer multiple cycles in which to achieve conception and the opportunity to have more than one pregnancy without further cost or risk. Hence tubal surgery and ART are not competitive but complimentary to each other.

References

1. Honore G M, Holder AE, Schenken RS.Pathophysiology and management of Proximal Tubal blockage. Fertil.Steril 1999; 5:785-795
2. Allahbadia G N, Merchant R. Fallopian tube recanalization: Lessons learnt and future challenges. Womens Health 2010; 4:531-548
3. Letterie GS, Sakes EL. Histology of proximal tubal obstruction in cases of unsuccessful tubal canalization. Fertil Steril 1991; 56:831-835
4. James C, Gomel V Surgical management of tubal factor in fertility. Curr.Opin.Obstet.Gynecol 1990;2:200-206
5. Molinas CR, Mynbaev O et al. Peritoneal mesothelial hypoxia during pneumoperitoneum is a cofactor in adhesion formation in a laparoscopic mouse model. Fertil Steril 2001; 76:560-567
6. Nackley AC,Mausher ST. The significance of hydrosalpinx in in vitro fertilization. Fertil Steril 1998;69:373-384.
7. Johnson N,van Voorst S, et al Surgical treatment for tubal disease in women due to undergo in vitro fertilization, Mol BWJ Cochrane Database of Systematic Reviews 2004, issue 3. Art No; CD002125.D0I:10.1002/14651858
8. Goynumer G,Kayabasoglu F,Aydogdu S,Wetherilt L.The effect of tubal sterilization through electrocoagulation on the ovarian reserve .Contraception 2009;80:90-94.
9. The Practice Committee of American Society of Reproductive Medicine. Role of Tubal Surgery in the era of Assisted Reproductive Technology: a committee opinion. Fertil Steril 2015;103:e37-43.
10. Rouzi, A.A, Mackinnon M, McComb P F,. Predictors of success of reversal of sterilization.Fertil.Steril,1995; 64: 29-36
11. Victor Gomel,The place of reconstructive tubal surgery in the era of assisted reproductive techniques Reproductive Biomedicine Online 2015; 31:722-731

Surrogacy: Rights Versus Law

Leena Wadhwa[1], Sanjana N Wadhwa[2], Ashish Fauzdar[3]
[1]Professor, [2]Senior Research Associate, [3]Scientist-I (Embryology), ESI-Post Graduate Institute of Medical Sciences & Research, Basaidarapur, Delhi

A *Surrogacy* agreement is an arrangement to carry a pregnancy for intended parents when pregnancy is either medically impossible or it is considered very risky for the mother's health. The word "surrogate," is rooted in Latin "Subrogare" (to substitute), which means "appointed to act in the place of." Surrogacy can be classified into two main types: *traditional and gestational*. *Traditional Surrogacy* involves impregnation of the surrogate naturally or artificially, and the resulting child is genetically related to the surrogate. In case of *Gestational Surrogacy,* pregnancy occurs due to the transfer of an embryo created by in vitro fertilization such that the resulting child is genetically unrelated to the surrogate. This can be *Commercial* or *Altruistic*. During *Commercial surrogacy* surrogate gets into an agreement to act as a surrogate mother and is paid over and above the necessary medical expenses. In *Altruistic* surrogacy a close relative that act as a surrogate mother receives no financial rewards for her pregnancy on the relinquishment of the child to the genetic parents except necessary medical expenses.

Commercial surrogacy is a controversial method of conception because people, governments and religious groups have questioned the ethics of involving money in a child's birth and the rights of surrogate mother, child and commissioning parents. This has also spiralled into unethical practices, putting life of both surrogate woman and their babies at risk. Over a period of time India had emerged as a leader in international surrogacy and a most sought after destination in surrogacy-related fertility tourism due to the relatively low cost of procedure and easy hiring and retention of Indian females as surrogates. Low-cost technology, skilled doctors, scant bureaucracy and a ready supply of surrogates made India a preferred destination for fertility tourism.

At present there are only draft guidelines formulated by Indian Council of Medical Research (ICMR)[1] for supervision between the Assisted Reproductive Technique (ART) banks, clinics and surrogates as the regulatory force. In a recent development health ministry has proposed legislation to prevent commercialization of surrogacy and to prohibit potential exploitation of surrogate mothers and protect the rights of children born through surrogacy.

History

Commercial surrogacy has been legal in India since 2002. In 2005 the first effort to regularize surrogacy in India was done by the Indian Council for Medical Research (ICMR) working under the Ministry of Health and Family Welfare. They finalized the National Guidelines for Accreditation, Supervision and Regulation of Artificial Reproductive Technology in India. In 2008 Manji case[2] made the headlines, which underscored the need for a regulatory framework for surrogacy in India. Baby Manji was commissioned by Japanese parents (through an unknown egg donor and the husband's sperm) and was born to a surrogate mother in Gujarat. The parents divorced before the baby was born. The genetic father wanted the child's custody, but Indian law barred single men from it, and Japanese law didn't recognize surrogacy. Finally, though the baby was granted a visa but the question of foreign surrogacy became especially relevant. In 2008, the Supreme Court of India in the Manji's case has held that though commercial surrogacy is permitted in India but pressed the requirement of legislature to pass an appropriate law governing surrogacy in India.

In year 2010 Indian Council of Medical Research (ICMR), under Ministry of Health & Family Welfare, Government of India revised the ART Guidelines including for surrogacy. As per these guidelines surrogacy was commercially allowed to help infertile patients. The guideline proposed to have written agreement for surrogacy between the prospective surrogate and the ART clinic explaining about the methods of treatment. Also mentioned in the contract is about the financial terms & conditions of the surrogacy between the ART bank & surrogate; between commissioning couple & the surrogate and agreement to hand over the child to parents after birth. All the documents are duly signed before with either of the parties with well-defined terms and conditions as per consent forms before being part of act of surrogacy.

There was another case highlighted by media in year 2012 where an Australian couple who had twins by surrogacy in INDIA, abandoned one healthy twin baby and took home the other.[3] In 2014, *Al Jazeera* carried a story which documented how Indian women were exploited in the name of commercial surrogacy.[4] Over the decades

there have been many incidents of unethical practices, exploitation of surrogate mothers who were forced to become surrogates many times in order to sustain their family, abandonment of children born out of surrogacy and import of human embryos and gametes. These incidents highlight the total disregard for the rights of the surrogate mother and child and have resulted in a number of public interest litigations in the Supreme Court to control commercial surrogacy.

Surrogacy, has been in the news due to many Bollywood celebrities such as Shah Rukh and Gauri Khan, Aamir and Kiran Rao Khan, and Sohail and Seema Sachdeva Khan who have all turned to surrogates to expand their families. ART for single parent is a controversial issue. Tusshar kappor being single, opted for ART with surrogacy for parenthood. It is worth noticeable all these cases gained attention during the time when there was no law been enacted by parliament regarding surrogacy. Due to this legal vacuum the misuse of certain guidelines of ICMR cannot be rated out in absence of concrete laws

Rights of a Surrogate Woman

There are number of ethical, social, legal and psychological issues associated with surrogacy, due to which an urgent need for framing and implementation of law was felt. Using multiple embryos increases health risks for the mother and babies. The hormones or drugs used for surrogate also have side-effects. Issues such as premature delivery, genetic malformation and infections which lead to increased hospitalization of surrogate and new-born are important issues to be considered. There are also certain health risk associated with surrogacy during pregnancy, birth and the post-partum period. This includes complications such as pre-eclampsia and eclampsia, life threatening haemorrhage, urinary tract infections, stress incontinence, gestational diabetes, and rarely pulmonary embolism.

A surrogate host of advanced maternal age has increased risk of perinatal mortality, intrauterine fetal death, neonatal death. Relinquishing the child may be extremely distressing and may result in psychological problems. In case of unfavorable outcome of pregnancy, the surrogates are unlikely to be paid, and there is no provision of insurance or post-pregnancy medical and psychiatric support for them.

Rights of Child

A child or children born to a married couple through the use of assisted reproductive technology shall be presumed to be the legitimate child of the couple, having been born in wedlock and with the consent of both spouses, and shall have identical legal rights as a legitimate child or children born through sexual intercourse. Sometimes people around surrogate mother give negative response and children born to are abandoned by their biological parents. Hence, left stateless and they are denied of their rights.

Since Gay rights are still an evolving issue in India and conferring legal rights to a surrogate child to gay parents would endanger the rights of the child itself. As far as homosexual relations and live in couples are concerned, such relations have no legal sanctity. Such people, including single parents, can go for adoption.

Exploitation of rural and tribal women

There is also need of laws to prevent exploitation of rural and tribal women due to lack of proper compensations and documentation. The commercial surrogacy exploits helpless poor women by taking advantage of their circumstances by paying less. There have been cases of pregnancies by way of surrogacy, including in rural and tribal areas, leading to possible exploitation of women by unscrupulous elements. These negative aspects of surrogacy on the society, surrogate mothers prompted to modify ART law and guidelines in safeguarding the right of surrogate mother. The poor, illiterate women of rural background are often persuaded to act as surrogates by their spouse or middlemen for earning easy money. Moreover, these women have no right on decision regarding their own body and life. In India, there is no provision of psychological screening or legal counseling, which is mandatory in western countries.[5]

Surrogacy Laws

Law Commission Observations[6]

In August, 2009 law commission of India had specifically reviewed the surrogacy law keeping in mind that India has emerged as International Surrogacy destination. The Law Commission of India has submitted the 228th Report on "NEED FOR LEGISLATION TO REGULATE ASSISTED REPRODUCTIVE TECHNOLOGY CLINICS AS WELL AS RIGHTS AND OBLIGATIONS OF PARTIES TO A SURROGACY." The following observations had been made by the Law Commission: -

(a) Surrogacy arrangement will continue to be governed by contract amongst parties, which will contain all the terms requiring consent of surrogate mother to bear child, agreement of her husband and other family members for the same, medical procedures of artificial insemination, reimbursement of all reasonable expenses for

carrying child to full term, willingness to hand over the child born to the commissioning parent(s), etc. But such an arrangement should not be for commercial purposes.

(b) A surrogacy arrangement should provide for financial support for surrogate child in the event of death of the commissioning couple or individual before delivery of the child, or divorce between the intended parents and subsequent willingness of none to take delivery of the child.

(c) A surrogacy contract should necessarily take care of life insurance cover for surrogate mother.

(d) One of the intended parents should be a donor as well, because the bond of love and affection with a child primarily emanates from biological relationship. Also, the chances of various kinds of child-abuse, which have been noticed in cases of adoptions, will be reduced. In case the intended parent is single, he or she should be a donor to be able to have a surrogate child. Otherwise, adoption is the way to have a child which is resorted to if biological (natural) parents and adoptive parents are different.

(e) Legislation itself should recognize a surrogate child to be the legitimate child of the commissioning parent(s) without there being any need for adoption or even declaration of guardian.

(f) The birth certificate of the surrogate child should contain the name(s) of the commissioning parent(s) only.

(g) Right to privacy of donor as well as surrogate mother should be protected.

(h) Sex-selective surrogacy should be prohibited.

(i) Cases of abortions should be governed by the Medical Termination of Pregnancy Act 1971 only.

This report highlighted a proper way of operating surrogacy in Indian conditions. The Law Commission strongly recommended against Commercial Surrogacy. However, this was a great step forward to the present situation.

In September, 2015 Ministry of Health and Welfare, invited suggestions from the public and stakeholders to address the revised draft of Assisted Reproductive Technology (Regulation) Bill, lacunae of existing Assisted Reproductive Technology (Regulation) Bill, 2010. The aim of these directions was to incorporate comment for safe and ethical practices before formulation of proper regulation for supervision of ART clinics and banks to prevent of misuse of technology including surrogacy before enactment of legislation. In the same year in November, 2015 Ministry of Health & family Welfare, Government of India took a policy decision not to support the commercial surrogacy as proposed "Assisted Reproductive Technology (Regulation) Bill" was still under consideration. This decision prohibited the import of human embryos for offering surrogacy services and not allowing visas to foreign nationals, overseas citizens of India (OCI) cardholders intending to visit India for commissioning surrogacy. These instructions were applicable to surrogacy Clinics/ART Clinics/IVF Clinics/Genetic Counseling Centers/Genetic Laboratories/ART Banks and other establishments and will remain in force till enactment of the legislation. On 24th August, 2016, the Union cabinet approved the Surrogacy (Regulation) Bill, 2016[5] and restricted surrogacy to Indian married infertile couples only and barring persons of Indian Origin, Non Resident Indians along with Overseas Citizen of India (OCI) for commissioning surrogacy in India.

Surrogacy Bill, 2016

The proposed draft Surrogacy Regulation Bill 2016, passed by the Health Ministry, was cleared by the Union Cabinet on the 24th of August 2016; and is set to be introduced in the Parliament soon. This bill was introduced to prevent exploitation of women and protecting rights of children born out of surrogacy. The government has totally prohibited foreigners from commissioning surrogacy in the country and has drafted this comprehensive legislation. The government also proposed that provisions are being made in the draft Bill to make parentage of children born out of surrogacy "legal and transparent".

Salient feature of the Surrogacy (Regulation) Bill 2016[7]:

1. To allow altruistic ethical surrogacy to intending infertile couple between the age of 23-50 years and 26-55 years for female and male respectively.
2. The intending couples should be legally married for at least five years and should be Indian citizens.
3. The intending couples have not had any surviving child biologically or through adoption or through surrogacy earlier except when they have a child and who is mentally or physically challenged or suffer from life threatening disorder with no permanent cure.
4. The intending couples shall not abandon the child, born out of a surrogacy procedure under any condition.
5. The child born through surrogacy will have the same rights as are available for the biological child.
6. The surrogate mother should be a close relative of the intending couple and should be between the age of 25-35 years. She can act as surrogate mother only once.

7. The surrogate mother will carry a child which is genetically related to the intending couple.
8. An order concerning the parentage and custody of the child to be born through surrogacy is to be passed by a court of the Magistrate of the first class.
9. An insurance coverage of reasonable and adequate amount shall be ensured in favour of the surrogate mother.
10. National Surrogacy Board shall exercise the powers and shall perform functions conferred on the Board under this Act.
11. The surrogacy clinics shall be registered under this Act after the Appropriate Authority is satisfied that such clinics are in a position to provide facilities and can maintain equipments and standards including specialized manpower, physical infrastructure and diagnostic facilities as may be prescribed in the rules and regulations.
12. No person, organisation, surrogacy clinic, laboratory or clinical establishment of any kind shall undertake commercial surrogacy, abandon the child, exploit the surrogate mother, sell human embryo or import embryo for the purpose of surrogacy. Violation to the said provision shall be an offence punishable with imprisonment for a term which shall not be less than ten years and with fine which may extend to ten lakh rupees.
13. The surrogacy clinics shall have to maintain all records for a period of 25 years.
14. Transitional Provision-Subject to the provisions of this Act, there shall be provided a gestation period of ten months from the date of coming into force of this act to protect the wellbeing of already existing surrogate mothers.

The proposed draft Surrogacy Bill 2016 has several checks on who is an eligible candidate for surrogacy, and also has restrictions on who can be a surrogate mother. The government, in this legislation, has also tried to define a couple in "need" for a surrogate child. The bill effectively bans foreigners to seek an Indian surrogate mother including non-resident Indians (NRIs). The proposed law allows only heterosexual married Indian couples with "proven infertility" to try the surrogacy route and keeps out homosexual couples as the law does not cover them, as well as live-in partners, and single men and women who might want a surrogate child.

Conclusions

The Union Cabinet approved the Surrogacy (Regulation) Bill 2016, banning commercial surrogacy in India. The surrogacy bill aims to prohibit potential exploitation of surrogate mothers and children born through surrogacy. It allows ethical altruistic surrogacy to the married infertile couples only. As of present situation India does not have any legislation governing ART even though guidelines drafted by Indian Council of Medical Research in this regard has been worked and reworked many times over last fifteen years. Yet these ART guidelines have not become law. Under this bill, matters involving surrogate mother's health, financial condition and psychological issues have been addressed. Still there remains a grey area which needs to be covered. Looking at today's scenarios of surrogacy, India needs to formulate ART laws through proper legal framework to protect rights of surrogates, child and commissioning couples.

Source of Support: Nil,

Conflict of Interest: None declared

References

1. Guidelines, Draft Assisted Reproductive Technologies (Regulation) Bill-2010.; (Available from *http://icmr.nic.in/About_Us/Guidelines.html)* accessed on December 12, 2016)
2. Baby Manji's case throws up need for law on surrogacy Dhananjay Mahapatra | TNN | Aug 25, 2008, 02.38AM accessed on December 12, 2016)
3. Shalini Nair. From abandonment to abuse, 18 cases that helped draft surrogacy bill. The Department of Health Research had submitted a report documenting 11 cases from across the globe and seven in India. Published On: September 8, 2016 2:21 Am http:// indianexpress. com / article / india / india-news-india / surrogacy - bill - commercial - ban - indian - cases - sushma- swaraj-abandonment - abuse - girl - abortion-3019329
4. Shaikh Azizur Rahman. Indian surrogate mothers suffer exploitation. http://www.aljazeera.com/news/asia / 2014/03/ indian - surrogate - mothers - suffer - exploitation - 20143276727538166.html
5. Saxena P, Mishra A and Sonia Malik. Surrogacy: Ethical and Legal Issues. Indian J Community Med. 2012 Oct-Dec; 37(4): 211–213.
6. Law commission of India (report no. 228), need for legislation to regulate assisted reproductive technology clinics as well as rights and obligations of parties to a surrogacy (Available at*: http://www.lawcommissionofindia.nic.in* accessed on December 12, 2016.)
7. The Surrogacy (Regulation) Bill, 2016 The Surrogacy (Regulation) Bill; (Available from *http://www.dhr.gov.in/sites/default/files/surrogacyregbill_0.pdf* accessed on December 12, 2016.)

Forthcoming Events

1. CME on 'Infertility and Assisted Reproduction' by Department of Obstetrics and Gynaecology & IVF and ART Centre, Maulana Azad Medical College, Delhi on 5th February, 2017. Interesting topics and recent advances would be discussed. Details at http://www.mamc.ac.in/

2. International Gynae Cancer Conference on 18th and 19th February 2017, in India Habitat Center. It is a two day program with workshop on first day and Conference on the second.

3. Second Maternal-Fetal Medicine Workshop is being organized by High Risk Pregnancy & Perinatology Programme, Deptt. of Obstetrics & Gynaecology, Maulana Azad Medical College, New Delhi, on 18th February, 2017.

Events Held

1. CME by Fetal Medicine and Genetics Subcommittee of the AOGD in association with North Delhi Obs & Gynae study Group on 3rd December, 2016 at Sunderlal Jain Hospital.

2. Women health awareness on PCOS and Kavach (women's safety programme) on 15th December, 2016 at Rukmani Devi Public School, Pitampura by Reproductive Endocrinology subcommittee of AOGD and Public Awareness Committee, FOGSI.

3. Residential Retreat for AOGD Members was held on 24th - 25th December, 2016, at Brahma Kumaris Om Shanti Retreat Centre, Manesar.

4. CME by Reproductive Endocrinology subcommittee of AOGD & Delhi Gyne Forum (North) on 27th December, 2016 at Fortis Hospital, Shalimar Bagh.

5. CME on 'Challenges in Maternal Fetal Medicine' by AOGD - Fetal Medicine and Genetics subcommittee on 29th December, 2016 at Fortis Lafemme.

6. AOGD monthly clinical meeting at Hindu Rao Hospital on 30th December, 2016. Interesting cases were discussed.

CME by Fetal Medicine and Genetics Subcommittee of the AOGD in association with North Delhi Obs & Gynae study Group on 3rd December, 2016 at Sunderlal Jain Hospital.

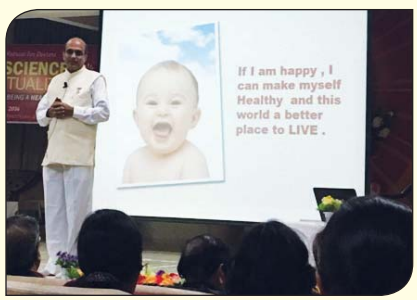
Women health awareness on PCOS and Kavach (women's safety programme) on 15th December, 2016 at Rukmani Devi Public School, Pitampura by Reproductive Endocrinology subcommittee of AOGD and Public Awareness Committee, FOGSI.

Women health awareness on PCOS and Kavach (women's safety programme) on 15th December, 2016 at Rukmani Devi Public School, Pitampura by Reproductive Endocrinology subcommittee of AOGD and Public Awareness Committee, FOGSI.

Women health awareness on PCOS and Kavach (women's safety programme) on 15th December, 2016 at Rukmani Devi Public School, Pitampura by Reproductive Endocrinology subcommittee of AOGD and Public Awareness Committee, FOGSI.

Residential Retreat for AOGD Members was held on 24th -25th December, 2016, at Brahma Kumaris Om Shanti Retreat Centre, Manesar.

Residential Retreat for AOGD Members was held on 24th -25th December, 2016, at Brahma Kumaris Om Shanti Retreat Centre, Manesar.



Residential Retreat for AOGD Members was held on 24th -25th December, 2016, at Brahma Kumaris Om Shanti Retreat Centre, Manesar.



Residential Retreat for AOGD Members was held on 24th -25th December, 2016, at Brahma Kumaris Om Shanti Retreat Centre, Manesar.


Residential Retreat for AOGD Members was held on 24th -25th December, 2016, at Brahma Kumaris Om Shanti Retreat Centre, Manesar.

CME by Reproductive Endocrinology subcommittee of AOGD & Delhi Gyne Forum (North) on 27th December, 2016 at Fortis Hospital, Shalimar Bagh

CME by Reproductive Endocrinology subcommittee of AOGD & Delhi Gyne Forum (North) on 27th December, 2016 at Fortis Hospital, Shalimar Bagh


CME on 'Challenges in Maternal Fetal Medicine' by AOGD - Fetal Medicine and Genetics subcommittee on 29th December, 2016 at Fortis Lafemme.

CME on 'Challenges in Maternal Fetal Medicine' by AOGD - Fetal Medicine and Genetics subcommittee on 29th December, 2016 at Fortis Lafemme.


AOGD Monthly Clinical Meeting at Hindu Rao Hospital on 30th December, 2016.



AOGD Monthly Clinical Meeting at Hindu Rao Hospital on 30th December, 2016.

12th National Conference of Indian Society of Colposcopy & Cervical Pathology

ISCCP CONFERENCE 2017

Date: **3rd -5th March, 2017** • *Venue:* **MAMC Auditorium, Delhi**
Pre - congress Workshop on 3rd March, 2017

SAVE THE DATES **3rd-5th March, 2017**
Cervical Cancer Prevention

Work shop highlights

1. Renowned international and national faculty
2. Update on cervical cancer screening
3. Videos on colposcopic techniques
4. Videos on normal and abnormal colposcopy
5. Videos on vulvoscopy
6. Videos on LEEP, (LETTZ),Cryotherapy, Conisation
7. **HAND's ON - LEEP EXPERIENCE**

Conference highlights

1. Renowned international and national faculty
2. HR HPV positive cases - What next ?
3. Recent guidelines on treatment of abnormal pap smear
4. Case discussions on management of CIN, & cervical cancer
5. Biomarkers and Immunohistochemistry in CIN & cancer cervix
6. Fertility sparing management of early cervical cancer
7. Videos of Radical Trachaelectomy and Ovarian Transposition
8. Management of Vulval and Vaginal lesions

Confirmed International Faculty


Dr Adeola Olaitan (UK)


Dr James Bently (USA)


Dr Partha Basu (France)


Dr Theresa Freeman-Wang (UK)

Dr Gauri Gandhi
Organizing Chairperson
ggandhi2004@yahoo.co.in
9968604344, 8860209017

For enquiries:
Dr Sumita Mehta- +91-9968609897, 9871014101
For Registration & Updates
www.isccp.in

Dr Sumita Mehta
Organizing Secretary
sumitadr@gmail.com
9968609897, 9871014101

Registration Fee

Registration Category	Upto 15th Dec, 2016	Upto 15th Feb, 2017	Spot Registration
ISCCP Member	Rs. 3800	Rs. 4200	Rs. 4500
ISCCP PG Student	Rs. 3200	Rs. 3500	Rs. 4000
ISCCP Non-Member	Rs. 4200	Rs. 4500	Rs. 5000
Accompanying Person	Rs. 3500	Rs. 4000	Rs. 4200

For queries, contact: **Dr Sumita Mehta**- +91-9968609897, 9871014101
Send Registration Form & details as mentioned above by post / courier to:
Dr Sumita Mehta, G-367, Preet Vihar, New Delhi-110092; E-Mail:- sumitadr@gmail.com

Story of Miss POLY PCOS .....

Kavita Agarwal[1], Narendra Malhotra[2], Jaideep Malhotra[3]

[1]Assistant Professor, Department of Obstetrics & Gynaecology, VMMC & Safdarjung Hospital, New Delhi; [2]Prof Dubrovnik International University, Managing Director Global Rainbow Health Care, Agra; [3]President Elect FOGSI 2018, Managing Director Rainbow IVF, Agra

One fine day a polycystic ovary syndrome (PCOS) woman gave birth to a chubby chubby baby girl Miss POLY PCOS ..... There is no clear cut mode of inheritance of PCOS. Initial studies suggested X - linked dominant transmission but recent studies say autosomal dominant inheritance. Risk of developing PCOS is 40% if sister is affected and 10 % if mother is affected.[1-6] Rapid weight gain in small for gestational age (SGA) girls in the first few years of life and sustained adiposity in large for gestational age (LGA) girls during childhood accelerate the prepubertal appearance of PCOS, characterized by visceral obesity, insulin resistance, and premature adrenarche/pubarche.[7-10]

Miss POLY PCOS has attained puberty.... Adolescent PCOS concerns are menstrual irregularities, obesity, hirsutism and acne. PCOS often manifests around the time of menarche as irregular and often lengthened menstrual cycles. Unfortunately, PCOS often goes unrecognized and undiagnosed at this time because having irregular periods in adolescence is usually considered normal by many relatives or health care professionals. These girls will often not receive a diagnosis until much later, perhaps at the time, when they seek treatment for infertility.

Lifestyle modifications, including a minimum of 30min of moderately intense exercise at least 3 days per week and dietary interventions is the first line treatment. A weight loss of 5–10% has been shown to decrease testosterone concentrations, increase SHBG, normalize menses, and improve fertility in women with PCOS. It can also attenuate insulin resistance and other metabolic aberrations. Prevention of excess weight gain should be emphasized in all women with PCOS with both normal & increased body weight.

Waxing, plucking, shaving, depilation, electrolysis, and laser hair removal techniques can all be used for hirsutism to remove current hair; however, pharmacological interventions are often needed to prevent new hair growth. Eflornithine cream (Vaniqa), an inhibitor of ornithine decarboxylase, is another option for the treatment of hirsutism, but it is expensive and needs to be used continuously to yield its desired effect. Unfortunately for the affected adolescent, it may take up to 12 months to reverse the androgen-induced transformation of vellus to terminal hairs and see clinical improvement in hirsutism due to the prolonged growth cycle of hair. For acne, topical treatment with salicylic acid, benzoyl peroxide, clindamycin/ benzoyl, peroxide preparations, isotretinoin, and clindamycin/ isotretinoin combinations can be used. If topical therapies for acne are ineffective, oral isotretinoin can be used. However, given its teratogenicity, isotretinoin is typically only used in severe cases of acne and in combination with effective forms of contraception.

Combined hormonal oral contraceptive pills (OCPs) containing both estrogen and progestin are the most common form of therapy in adolescents with PCOS, improving hirsutism, acne, and menstrual irregularity. The estrogen component suppresses Leutinizing hormone (LH) secretion (and thus ovarian androgen production) and increases hepatic sex hormone binding globulin production (decreasing the amount of free testosterone); the progestin component protects the endometrium from unopposed estrogen. The choices available are

1. OCPs with standard progestin (Mala, Ovral) for adolescents with AUB alone or associated with hyperandrogenic features.
2. OCPs with the fourth-generation progestin drospirenone (Yasmin 30 mcg of ethinyl estradiol with 3 mg drospirenone] and Yaz [20 mcg of ethinyl estradiol with 3 mg drospirenone]) is preferred in obese girls with or without hirsutism because it is a derivative of spironolactone and thus has direct antiandrogenic activity and has antimineralocorticloid activity which minimizes weight gain and may have temporary weight losing effect.
3. OCP with cyproterone acetate 2mg (Diane, Krimson); desogestrel (Novelon) which are antiandrogenic are suitable for girls with predominant hyperandrogenic features.

If hirsutism is not controlled by cosmetic and OCP treatment, antiandrogen therapy is added. Spironolactone, competitive androgen receptor (AR) antagonist is the drug of choice at a dose of 100–200 mg/day in divided doses. The AR inhibitor

flutamide; Finasteride, a 5a-reductase inhibitor, is another antiandrogen for the treatment of hirsutism. Anti obesity drugs like Sibutramine and orlistat can be considered in morbidly obese patients (BMI>30). Bariatric surgery can play role in women with extremely high, life threatening BMI. Insulin-sensitizer metformin can be added in adolescents with impaired glucose tolerance, insulin resistance, and/or obesity.[11,12] The optimum dose is 1500-2000mg per day and is best tolerated as extended release twice daily schedule. The thiazolidinediones (TZDs) (troglitazone, rosiglitazone, and pioglitazone) are another class of insulin-sensitizing agents but they can lead to weight gain, heart failure, hepatocellular toxicity. Hence are not advocated in adolescents.

Miss POLY PCOS is now 24 year old Mrs. POLY PCOS. She is newly married and does not want pregnancy... Her other concerns are obesity, hirsutism and oligomenorrhoea. The best treatment option for her after lifestyle management is the third generation oral contraceptive pills. Low dose estrogen with drosperinone/ cyproterone acetate are preferred contraceptive pills for her. The advantages are cycle regularisation, no weight gain, control androgenic symptoms and effective contraception.

Mrs POLY PCOS wants to conceive now.... Infertility in PCOS is due to infrequent or absent ovulation. Prior to conception, the importance of folate, smoking cessation, weight loss and optimal exercise needs to be emphasized. Introduction of diet and lifestyle changes alone can improve fertility and should be considered before attempting ovulation induction in women with PCOS.[13] According to PCOS treatment algorithm by ESHRE/ASRM consensus workshop,[13] after preconceptional counseling on life style modification, clomiphene citrate (CC) is the first line treatment for ovulation induction followed by gonadotropins, laparoscopic ovarian drilling and In Vitro Fertilisation (IVF) as the third line of treatment. Ovarian stimulation in PCOS is of concern as response, dose and number of days of stimulation is not predictable. Control over the cycle is difficult and Ovarian Hyperstimulation syndrome is a real problem.

Clomiphene citrate increases FSH, thereby inducing follicular growth and ovulation. 75-80%[14] will ovulate but conception rate 22% per cycle[15] in those ovulating with Clomiphene. That is, despite the high rates of ovulation, pregnancy rates per cycle remain relatively low with the use of Clomiphene. An antiestrogenic effect of Clomiphene on the endometrium has been postulated.[16,17]

There is no evidence that addition of corticosteroids or bromocriptine has any improvement in pregnancy rates. Hence empirical use of these agents has now been abandoned. *Corticosteroids* can be added only in cases where there is an increased DHEAS levels, as this will suggest an increase in the adrenal androgens which is sometimes seen in patients of PCOS. In patients with normoprolactinemic anovualtion, but with presence of galactorrhoea, can be given *Bromocriptine* if therapy with CC alone fails. Use of bromocriptine is reserved for hyperprolactinemic anovulation. CC compared with metformin alone results in higher ovulation, conception, pregnancy & live birth rate. CC + Metformin results in no substantial benefits except, patients with BMI >35 or abnormal GTT.[13,18] Aromatase inhibitor like letrozole is an off label drug and not to be used.

When CC fails, the second line option available is the use of gonadotropins for the treatment of anovulation. Also gonadotropins alone give good results than CC combined with gonadotropins. Laparoscopic ovarian surgery (LOS) with monopolar coagulating current, 40 W power, not more than 4 punctures made for 2-3 sec at each point can be tried in CC resistance cases, especially in lean women, women with hypersecretion of LH, high levels of androstenedione and previous over response to controlled ovarian hyperstimulation for IVF.[19,20] However, with LOS alone ovulation rate is >80% but <50% clomiphene – resistant women conceive.[21]

IVF is useful in patients with failed gonadotropin therapy or with additional causes of infertility, such as male factor infertility. The stimulation protocols have to be individualized. Pure & recombinant gonadotropin are preferred. FSH dose should be tailored on the basis of ovarian reserve markers (the higher the ovarian reserve, the lower the dose). For hyper-responders, low dose FSH 150 IU is preferred. Using very high FSH stimulation is useless in poor responders (300 IU is sufficient). Both GnRH agonist long protocol and GnRH Antagonist protocol gives equal results in poor responders. However, to prevent OHSS, a GnRH antagonist protocol is the first choice in PCOS hyper responders.[22] Also, with GnRh antagonist, significantly less gonadotropin is required and better compliance is there due to less number of injections. Also, GnRH agonist triggering is a valid alternative to hCG triggering, resulting in an elimination of risk of OHSS.[23,24] Folicular monitoring by ultrasound and estradiol assessment are ideal for safe and effective monitoring of ovulation induction.

Mrs POLY PCOS is pregnant. During pregnancy, risks involve recurrent miscarriages in 50%

women, gestational diabetes, pregnancy induced hypertension, Intra uterine growth restriction.[25,26] Some studies have shown that continuing metformin in pregnancy may decrease the rate of miscarriage, gestational diabetes requiring Insulin, pre eclampsia, intra uterine growth restriction but none of these are prospective, randomized trials. Randomized controlled trials are needed in this area before sustained metformin treatment throughout pregnancy can be recommended. For screening of gestational diabetes, these women should have 75gm oral glucose tolerance test done in every trimester as per latest DIPSI/ IDA guidelines. Women should have regular antenatal check ups and be monitored as any other high risk pregnancy.

Mrs POLY PCOS has one child and wants spacing. Oral contraceptives are the best option for them but if wish to use other contraceptive then ensure 2 monthly withdrawl to avoid long term complications of unopposed estrogen actions on the endometrium.

Mrs POLY PCOS has abortions, one child, now want another one and is not conceiving (secondary infertility). Life style modification is the first line of treatment. Evaluate her for other causes of infertility, tubal, uterine or male factor. If anovulatory, ovulation induction protocols to be given. If with recurrent pregnancy loss with no other causes, suppressing leutinizing hormone/ insulin sensitizer/GnRH agonist can be tried.

Mrs POLY PCOS has completed family. Mature PCOS coming back again in the form of menstrual irregularities, hirsutism, acne, lethargy and obesity. She is predisposed to metabolic syndrome, Type 2 Diabetes, hypertension, atherosclerosis, coronary artery disease, severe oligomenorhoea/ amenorrhoea, increased incidence of endometrial cancer, epilepsy and sleep apnoea. She would require regular blood pressure measurement, fasting blood sugar and OGTT periodically, lipid profile and homocysteine levels.

Mrs POLY PCOS in menopausal, has developed all long term complications, metabolic syndrome. She should be advised life style management, insulin sensitizers, antihypertensives and statins.

Newer available drugs are melatonin, myoinositol, N- acetyl cysteine, L- methyl folate, alfa- calcidol and chromium. The basis of newer drugs use is that insulin resistance contributes to oxygen stress. Reactive oxygen species are produced within the follicles, especially during the ovulation process. Oxidative stress affects oocyte maturation leading to poor oocyte quality and embryo development. Also, oxidative stress affects leutinization and hence, there is decreased progesterone production and luteal phase defect. Thus, oxidative stress affects the whole of reproductive cycle from oocyte maturation, embryo development to implantation. Melatonin, secreted by pineal gland, is taken up into the follicular fluid from the blood. Reactive oxygen species, produced within the follicles, are scavenged by melatonin. Melatonin reduces intra-follicular oxidative damage, prevents lipid peroxidation, protein, and DNA damage, thereby elevating fertilization and pregnancy rates. Myoinositol is available as a diet supplement. It plays a role in insulin signalling thereby increasing insulin sensitivity. A dose of 3-4 gms for 3-6 months can improve ovulatory function. However, there are yet no randomized clinical trials to prove their efficacy in PCOS women.

To summarize, PCOS is a complex and frequent disorder with a heterogeneous clinical presentation varying throughout life, from birth up to post-menopause. When a young patient presents with hirsutism and irregular periods, the health care provider should always be alerted to the possibility of PCOS. Management is age and need oriented. Early intervention through lifestyle modification is the crux. Prevention of long term medical co morbidities, metabolic syndrome should always be kept in mind.

References

1. Legro R, Driscoll D, Strauss 3rd JF, Fox J, Dunaif A. Evidence for a genetic basis for hyperandrogenism in polycystic ovary syndrome. Proc Natl Acad Sci USA 1998;95:14956–1460.
2. Goodarzi MO, Guo X, Yildiz BO, Stanczyk FZ, Azziz R. Correlation of adrenocorticotropin steroid levels between women with polycystic ovary syndrome and their sisters. Am J Obstet Gynecol 2007;196:398 e1–e5.
3. Baillargeon JP, Carpentier AC. Brothers of women with polycystic ovary syndrome are characterised by impaired glucose tolerance, reduced insulin sensitivity and related metabolic defects. Diabetologia 2007;50:2424–2432.
4. Franks S, Webber LJ, Goh M, Valentine A, White DM, Conway GS, Wiltshire S, McCarthy MI. Ovarian morphology is a marker of heritable biochemical traits in sisters with polycystic ovaries. J Clin Endocrinol Metab 2008; 93: 3396–3402.
5. Sam S, Coviello AD, Sung YA, Legro RS, Dunaif A. Metabolic phenotype in the brothers of women with polycystic ovary syndrome. Diabetes Care 2008;31:1237–1241.
6. Kent SC, Gnatuk CL, Kunselman AR, Demers LM, Lee PA, Legro RS. Hyperandrogenism and hyperinsulinism in children of women with polycystic ovary syndrome: a controlled study. J Clin Endocrinol Metab 2008;93: 1662–1669.

7. Ibanez L, Diaz R, Lopez-Bermejo A, Marcos MV. Clinical spectrum of premature pubarche: Links to metabolic syndrome and ovarian hyperandrogenism. Rev Endocr Metab Disord 2009;10:63–76.
8. Dunaif A. Insulin action in the polycystic ovary syndrome. Endocrinol Metab Clin North Am 1999;28:341–359.
9. Ibanez L, Lopez-Bermejo A, Callejo J, Torres A, Cabre S, Dunger D, de Zegher F. Polycystic ovaries in nonobese adolescents and young women with ovarian androgen excess: relation to prenatal growth. J Clin Endocrinol Metab 2008; 93:196–199.
10. Ibanez L, Valls C, Potau N, Marcos MV, de Zegher F. Polycystic ovary syndrome after precocious pubarche: Ontogeny of the low-birthweight effect. Clin Endocrinol (Oxf) 2001; 55: 667–672.
11. Palomba S, Falbo A, Zullo F, Orio F Jr. Evidence-based and potential benefits of metformin in the polycystic ovary syndrome: a comprehensive review. Endocr Rev 2009; 30: 1–50.
12. Diamanti-Kandarakis E, Christakou CD, Kandaraki E, Economou FN. Metformin: An old medication of new fashion: Evolving new molecular mechanisms and clinical implications in polycystic ovary syndrome. Eur J Endocrinol 2010; 162:193–212.
13. Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2008) Consensus on infertility treatment related to polycystic ovary syndrome. Hum Reprod.2013; 23(3): 462–77.
14. Messinis IE. Ovulation induction: a mini review. Hum Reprod. 2005; 20(10): 2688–97.
15. Eijkemans MJ, Polinder S, Mulders AG, Laven JS, Habbema JD, Fauser BC. Individualized cost-effective conventional ovulation induction treatment in normogonadotrophic anovulatory infertility (WHO group 2) Hum Reprod. 2005; 20(10): 2830–7.
16. Brown J, Farquhar C, Beck J, Boothroyd C, Hughes E. Clomiphene and anti-estrogens for ovulation induction in PCOS. Cochrane Database Syst Rev. 2009;4:CD002249.
17. Ahlgren M, Källen B, Rannevik G. Outcome of pregnancy after clomiphene therapy. Acta Obstet Gyn Scan. 1976; 55(4): 371–5.
18. Tang T, Lord JM, Norman RJ, Yasmin E, Balen AH. Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, D-chiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility. Cochrane Database Syst Rev. 2012; 5:CD003053.
19. Balen A. Ovulation induction in the management of anovulatory polycystic ovary syndrome. Mol Cell Endocrinol. 2013; 373((1-2)):77–82.
20. Farquhar C, Brown J, Marjoribanks J. Laparoscopic drilling by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome. Cochrane Database Syst Rev.2014;6: CD001122.
21. Unlu C, Atabekoglu CS. Surgical treatment in polycystic ovary syndrome. Curr Opin Obstet Gynecol. 2006; 18(3): 286– 92.
22. Al-Inany HG, Youssef MA, Aboulghar M, Broekmans F, Sterrenburg M, Smit J, et al. Gonadotrophin-releasing hormone antagonists for assisted reproductive technology. Cochrane Database Syst Rev. 2011;5: CD001750.
23. Xiao J, Chen S, Zhang C, Chang S. Effectiveness of GnRH antagonist in the treatment of patients with polycystic ovary syndrome undergoing IVF: a systematic review and meta analysis. Gynecol Endocrinol. 2013; 29(3):187–91.
24. Griesinger G, Schultz L, Bauer T, Broessner A, Frambach T, Kissler S. Ovarian hyperstimulation syndrome prevention by gonadotropin-releasing hormone agonist triggering of final oocyte maturation in a gonadotropin-releasing hormone antagonist protocol in combination with a "freeze-all" strategy: a prospective multicentric study. Fertil Steril.2011; 95(6): 2029–33.
25. Boomsma CM, Eijkemans MJ, Hughes EG, Visser GH, Fauser BC, Macklon NS. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. Hum Reprod Update. 2006;12(6):673–83.
26. Qin JZ, Pang LH, Li MJ, Fan XJ, Huang RD, Chen HY. Obstetric complications in women with polycystic ovary syndrome: a systematic review and meta-analysis. Reprod Biol Endocrinol. 2013;11:56.

Successful Case of Pregnancy in XY Female: A case report

Kaberi Banerjee
Clinical Director, Advanced Fertility and Gynaecology Centre, New Delhi

Abstract

A case of 29-year old woman with androgen insensitivity syndrome came with infertility in which pregnancy was achieved with donor egg surrogacy. Oocytes were taken from donor and then fertilized with husband's sperm in laboratory. The embryos formed were transferred in surrogate's uterus and pregnancy was positive after 2 weeks.

Introduction

The new reproductive technologies, such as IVF ICSI, surrogacy are becoming increasingly common, enabling infertile couples to become parents and create families. One of the rare causes of female infertility is XY female disorder, which is characterized by chromosomal composition of 46 XY and female phenotype. There are different varieties of presentations. Androgen insensitivity syndrome is one of the causes of XY female occurring in around 1 in 22,000 to 60,000 births.[1] In the present case of Androgen insensitivity syndrome, there was a successful pregnancy in the surrogate after using donor eggs and husband's sperms.

Case Report

A 29 years old female came to our OPD with primary amenorrhea and primary infertility. We had advised the hormonal profile and the abdominal ultrasound. Serum hormonal measurements were FSH: 66.9 IU/ml, LH: 33.7 mIU/L, estradiol: 45 pg/ml, prolactin: 9.1 ng/ml, thyroid stimulating: 2.3 pg/ml. Ultrasound showed absent ovaries and uterus. The chromosomal analysis reveales a 46, XY karyotype. The husband's semen analysis was normal. She was diagnosed as a case of Androgen insensitivity syndrome.

In view of the above diagnosis, we recommended donor egg surrogacy to the couple. We stimulated the ovaries of donor with the highly purified menotrophin HMG 300 IU (hpHMG, Menopur; Ferring GmbH, Germany). After seven days of stimulation, transvaginal scan showed 10 good follicles of 14mm size in both ovaries. After that daily subcutaneous injection of GnRH antagonist, 0.25 mg Cetrorelix (Cetrotide, Merck Serono S.p.A, Italy), was added. When follicles reached 18 mm, 500 mcg recombinant hCG (rhCG, Ovitrelle; Merck Serono S.p.A, Italy) was given to trigger ovulation.

Transvaginal oocyte aspiration of ovaries was performed after 36 h, under ultrasound guidance, using Wallace OPU needle and Cooks gamete buffer media. We retrieved 10 oocytes and which were fertilized in the laboratory in Cooks fertilization media. Embryos were further cultured in cleavage media. Eight good embryos (grade A) were formed out of which three embryos were transferred in the surrogate and five embryos were frozen in two vials.

Surrogate preparation

GnRH agonist 0.5 mg Inj. Leuprolide Acetate (Lupride, Inca Sun Pharmaceutical Industries Ltd.) was started on day 21 of previous cycle and reduced to half dose (0.25 mg) on day 2 of next cycle along with addition of 6 mg estradiol valerate (Progynova, Zydus Cadila Healthcare Ltd., German Remedies) in divided doses. Transvaginal sonography for endometrial thickness was done on day 12 which was 9 mm. GnRH agonist injection was stopped after the trigger injection of the patient and Tablet estradiol valerate was continued in the same dose. Progesterone suppositories 200 mg (Naturogest, Zydus Cadila Healthcare Ltd., German Remedies) twice daily were started from the oocyte retrieval day of the patient. Three Day 2 Embryos were transferred in the surrogate. After 14 days of luteal support, beta HCG was done which came positive. Ultrasound was done after two weeks of beta HCG that showed intrauterine single live pregnancy of six weeks.

Discussion

Disorders of sex development (DSD) refer to a collection of congenital conditions in which atypical development of sex occurs at one or more levels (chromosomal, gonadal, anatomic).[2] There are two types of 46 XY DSD – one is Swyer syndrome, which is characterized by female phenotype with normal mullerian structures and bilateral streak gonads. Other type is Androgen insensitivity syndrome, which is characterized by female phenotype with absent or rudimentary mullerian structures and bilateral atrophic

testes in abdomen or inguinal region.[3] Infertility is an important management issue; however, pregnancy may be feasible through zygote egg donation and surrogacy.[4]

In our case report, pregnancy was only possible with donor egg with surrogacy.

Conflicts of interest: This is to certify that there is no conflict of interest regarding the publication of this manuscript.

References

1. Quigley CA, De Bellis A, Marschke KB, el-Awady MK, Wilson EM, French FS. "Androgen receptor defects: historical, clinical, and molecular perspectives". Endocr. Rev. 1995; 16 (3): 271–321.
2. Wisniewski AB, Mazur T. 46,XY DSD with Female or Ambiguous External Genitalia at Birth due to Androgen Insensitivity Syndrome, 5*α*-Reductase-2 Deficiency, or 17*β*-Hydroxysteroid Dehydrogenase Deficiency: A Review of Quality of Life Outcomes. International Journal of Pediatric Endocrinology. 2009; 2009: 567430. doi:10.1155/2009/567430.
3. Galani A, Kitsiou-Tzeli S, Sofokleous C, Kanavakis E, Kalpini-Mavrou A. Androgen insensitivity syndrome: clinical features and molecular defects. Hormones (Athens). 2008; 7(3): 217-29.
4. Hughes IA, Davies JD, Bunch TI, Pasterski V, Mastroyannopoulou K, MacDougall J. Androgen insensitivity syndrome. Lancet. 2012; 380: 1419-28.

AOGD Sub Committee Nomination (2017-19)

Nominations are invited for the post of **chairperson** of the following sub-committees for the year 2017-19:-

1. ADOLESCENT HEALTH
2. ENDOSCOPY
3. ENDOMETRIOSIS
4. FETAL MEDICINE & GENETICS
5. ONCOLOGY
6. REPRODUCTIVE ENDOCRINOLOGY
7. SAFE MOTHERHOOD
8. UROGYNAECOLOGY

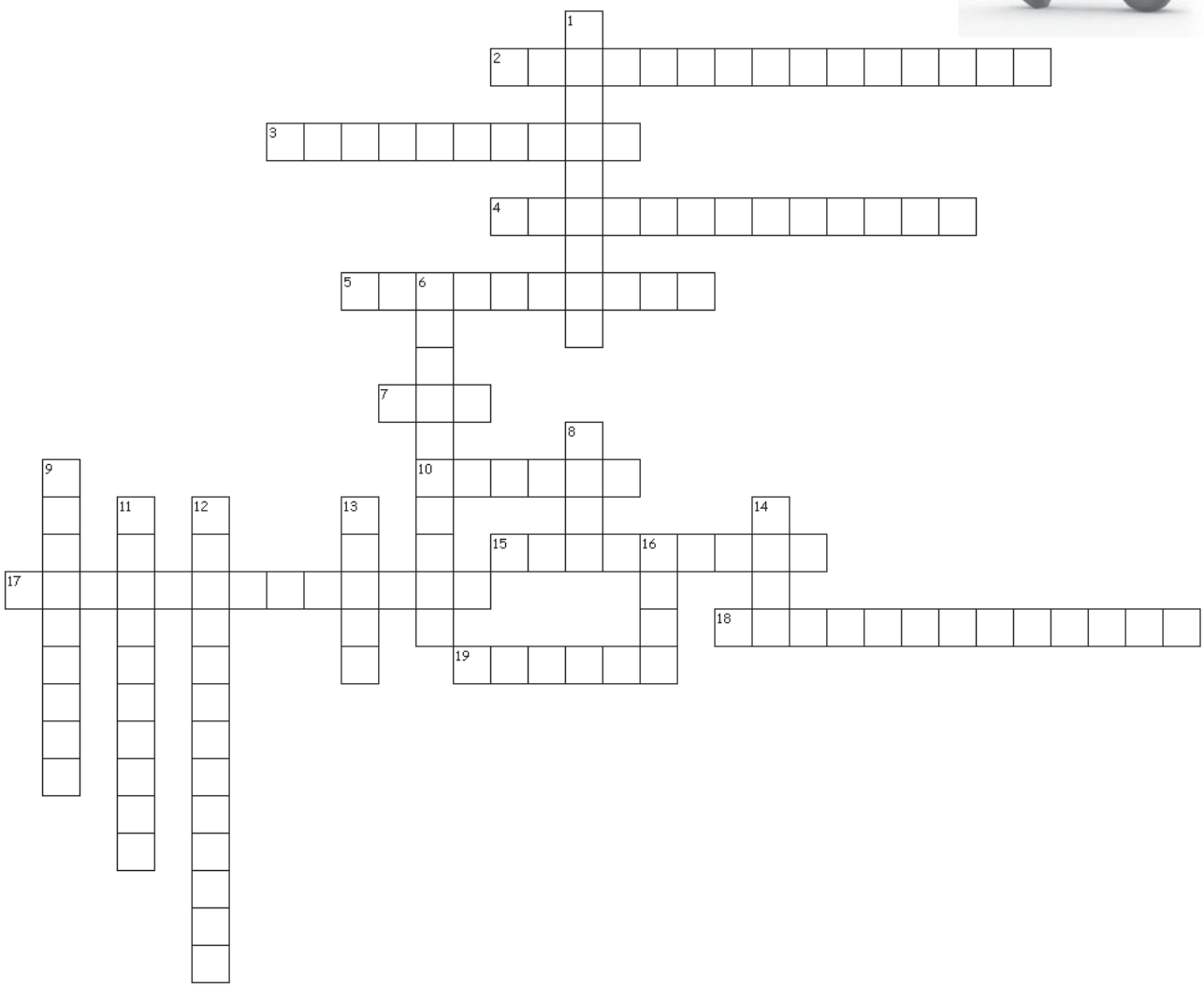
Eligibility Criteria

1. Person should be a member of AOGD and have at least 10 years standing in the profession with at least 5 years duration of holding senior position in the respective institutions.
2. Chairperson of a subcommittee has to be a member of any subcommittee earlier for at least 1 year.
3. No repeat nomination will be considered after one term of two years.
4. In case of two people applying for the same post, the decision of the executive will be final.
5. In case of any deviation, the decision would be taken by executive committee.
6. Two posts cannot be held by any member at one particular time.

The nominations on plain paper should reach:
AOGD Secretariat: Guru Teg Bahdur Hospital, New Delhi by 10th April, 2016 along with the bio-data stating the eligibility.

Crossword - Infertility

Compiled and designed by Ashwathy Kumaran[1], Sangeeta Gupta[2]
[1]FNB Fellow, Reproductive Medicine, [2]Professor, Obstetrics & Gynecology, Maulana Azad Medical College, New Delhi, India



Across

2. Long acting FSH agonist
3. A drug that stimulates more FSH and LH release from the pituitary, stimulating growth of an ovarian follicle.
4. Surgical formation of an opening in a fallopian tube whose fimbriated extremity has been closed as a result of inflammation
5. Latest SPRM
7. Test to determine implantation window (Abbreviation)
10. LH stimulates _____ cells in the testes to produce testosterone
15. A biguanide oral hypoglycaemic used in the treatment of PCOS
17. Excess of abnormal forms of sperm
18. The probability that conception is achieved for every month of exposure is defined as _____
19. A gestational mother provides only her ____

Down

1. Cells that produce inhibin B which negatively feedback the anterior pituitary.
6. Improves implantation by acting on NK cells
8. Which assisted reproductive technology places collected oocytes and sperm in the woman's fallopian tubes? (Abbreviation)
9. Nerve responsible for erection, can be damaged in surgical removal of prostate
11. First uterine transplant done by _____
12. Estradiol peaks during which uterine phase?
13. Name of first Indian IVF baby is _____
14. Jaycee Buzzanca had ____ parents
16. A complication of treatment resulting in a syndrome involving swelling and pain in ovaries (Abbreviation)

(..... answers to crossword on page 40)

Journal Scan

Deepti Goswami
Director-Professor, Department of Obstetrics & Gynaecology, Maulana Azad Medical College & Lok Nayak Hospital, New Delhi

Abstract of the research articles are available free at the journal websites and on PubMed (http://www.ncbi.nlm.nih.gov/pubmed). A summary of the articles has been provided so as to put the findings of the articles into perspective for current clinical practice.

First live birth using human oocytes reconstituted by spindle nuclear transfer for mitochondrial DNA mutation causing Leigh syndrome

Zhanga J, Liua H, Luob S, Chavez-Badiolac A, Liua Z, Yang M, Munned S, Konstantinidisd M, Wellse D, Huangf T

Citation: Zhanga J, Liua H, Luob S, Chavez-Badiolac A, Liua Z, Yang M, Munned S, Konstantinidisd M, Wellse D, Huangf T. First live birth using human oocytes reconstituted by spindle nuclear transfer for mitochondrial DNA mutation causing Leigh syndrome. Fertil Steril 2016 Sep; 106 (3) Suppl : e375–e376

Study Question: Experimental nuclear transfer in metaphase II (MII) spindle oocytes or in pronuclear (PN) zygotes, also called mitochondrial replacement therapy, has been shown to be a novel technology in minimizing mutated mtDNA transmission from oocytes to pre-implantation embryos. The authors report the first live birth of a boy following spindle nuclear transfer (SNT).

Methods

- The patient is a 36-year-old woman who carries genes for Leigh syndrome, a fatal mitochondrial disease that affects the developing nervous system. Nearly one fourth (24.5%) of her mitochondria have the disease-causing mutation.
- She is healthy; however she had suffered 4 pregnancy losses including two children affected by Leigh syndrome.
- Patient's spindle nuclei were isolated and transferred into the perivitelline space of enucleated donor oocytes.
- The micro-manipulated complexes were then subjected to 1.4 kV/cm DC voltage for cell membrane fusion.
- The reconstituted oocytes were fertilized by intracytoplasmic sperm injection (ICSI).
- The developed blastocysts were biopsied for preimplantation genetic screening by array comparative genetic hybridization and whole quantitative genomic mtDNA analysis by Next Generation Sequencing.

Results

- Five M II oocytes with birefringent spindles were subjected to meiotic SNT.
- The 5 oocytes were successfully reconstituted and fertilized normally by ICSI.
- Four out of 5 fertilized oocytes developed into blastocysts.
- PGS showed that one blastocyst was euploid (46XY), while 3 embryos were aneuploid.
- Transfer of the euploid embryo resulted in an uneventful pregnancy with delivery of a healthy boy at 37 weeks of gestation.
- The average level of transmitted mother's mtDNA in several neonatal tissues including buccal epithelium, hair follicles, circumcised foreskin, urine precipitate, placenta, amnion, umbilical blood, and umbilical cord was less than $1.60 \pm 0.92\%$.
- The baby was doing well at 3 months of age.

Conclusion

Human oocytes reconstituted by SNT are capable of producing a healthy live birth. SNT may provide a novel treatment option in minimizing pathogenic mtDNA transmission from mothers to their babies.

Perspective

This "breaking news" category of abstract was presented at the meeting of American Society of Reproductive Medicine (ASRM) 2016. This is the first reported birth of a "3- parent baby" as the baby received genes from father, mother and a female donor. This work was carried out by American doctors working at a clinic in Mexico and the beneficiary were a Jordanian couple where the woman carried genes for Leigh syndrome (a mitochondrial disease).

Mitochondrial diseases result due to mutations in mitochondrial DNA and can cause fatal heart problems, liver failure, brain disorders, blindness and muscular dystrophy. They are estimated to affect 1 in 4000

people. This technology adds a new dimension to the fertility management for families at risk of transmitting mitochondrial diseases. Britain's parliament voted last year to allow this three-parent in-vitro-fertilization technique involving mitochondrial transfer. An independent expert panel of the Human Fertilization and Embryology Authority (HFEA) has opined that this technique should now be approved by the HFEA for "cautious" use in "specific circumstances."

Note: *This abstract is not available on Pubmed but can be accessed in the print journal.*

Effect of first line cancer treatment on the ovarian reserve and follicular density in girls under the age of 18 years

El Issaoui M, Giorgione V, Mamsen LS, Rechnitzer C, Birkebæk N, Clausen N, Kelsey TW, Andersen CY

Citation: El Issaoui M, Giorgione V, Mamsen LS, Rechnitzer C, Birkebæk N, Clausen N, Kelsey TW, Andersen CY. Effect of first line cancer treatment on the ovarian reserve and follicular density in girls under the age of 18 years. Fertil Steril.2016 Dec;106(7):1757-1762.e1.

Study Question: What is the potential gonadotoxic insult caused by a first-line cancer treatment on the fertility potential in prepubertal and adolescent girls?

Methods

- This retrospective case-control study involved girls referred to one of the three centers involved in the Danish program for ovarian tissue cryopreservation (OTC) between the years 2002 and 2014.
- Subjects included sixty-three girls under the age of 18 (range: 1.5–17.9) years who underwent OTC before (group 1: 31 patients) and after (group 2: 32 patients) their initial cancer treatment.
- Main outcome measure was follicular densities (follicles/mm3) measured from an ovarian cortical biopsy before OTC. The ovarian volume (mL) of entire ovaries excised for OTC was also monitored.

Results

- There was no statistically significant difference in the mean age or follicular density between groups 1 and 2 (334 ± 476/mm3 vs. 327 ± 756/mm3).
- In contrast, the ovarian volume and total number of ovarian cortex chips cryopreserved were statistically significantly lower in patients who received gonadotoxic treatment before OTC (mean ± standard deviation [SD]: ovarian volume, 5.3 ± 3.1 mL vs. 2.9 ± 2.1 mL, respectively; number of cortex chips: 21.3 ± 8.1 vs. 15.2 ± 7.1, respectively).
- The reduction in the estimated ovarian reserve ranged from 10% to 20% in children to around 30% in adolescent girls (>10 years).

Conclusion

Girls under the age of 10 tolerate a gonadotoxic insult better than adolescents, who may experience up to a 30% reduction in the ovarian reserve via first-line gonadotoxic treatment, which at present is considered to have little effect on the follicle pool. This information will improve counseling of young female cancer patients in deciding whether to undergo fertility preservation treatment.

Perspective

There is always a concern about the future fertility potential of young girls receiving chemotherapy for malignancies since the chemotherapeutic drugs are gonadotoxic and cause premature ovarian insufficiency. Ovarian tissue cryopreservation is the only option for preserving fertility for prepubertal girls. The fertility preservation intervention is recommended when the estimated risk of premature ovarian insufficiency is more than 50%. However it is often difficult to decide whether it is necessary to do invasive procedure to obtain ovarian tissue for cryopreservation in these young girls. The results of this study would help in counseling the parents of these young patients regarding whether ovarian tissue preservation should be performed or not.

Calendar of Monthly Clinical Meetings 2016-17

Months	Name of the Institute
January, 2017 (03.02.2017)	LHMC
February, 2017	ESI Hospital
March, 2017	UCMS & GTB Hospital
April, 2017	Apollo Hospital

Case Summaries for AOGD Bulletin may be sent by email to the editor/CD may be handed over on the day of the meeting.

-Dr Sangeeta Gupta

HISTORY

Infertility: An ancient taboo to women!

Nilanchali Singh, Nupur Ahuja
Department of Obstetrics and Gynaecology, Maulana Azad Medical College

Infertility is learning to live in grief, while still finding a way to a fulfilling life.

Infertility has been a major medical and social preoccupation since the dawn of human existence and women have always been the symbol of fertility. Since antiquity, couples have been prolific and difficulty with conception was a real problem.

In Egyptian society, women were equal to men, and difficulty with conception was not considered divine punishment but an illness that had to be diagnosed and treated. As far back as 1900 BC, there are recorded documents discussing the treatment of gynaecologic disorders.

One of the main sources of knowledge concerning Jewish medicine in ancient times is the Bible. The notion of original sin predominated and women had very few rights or liberties.

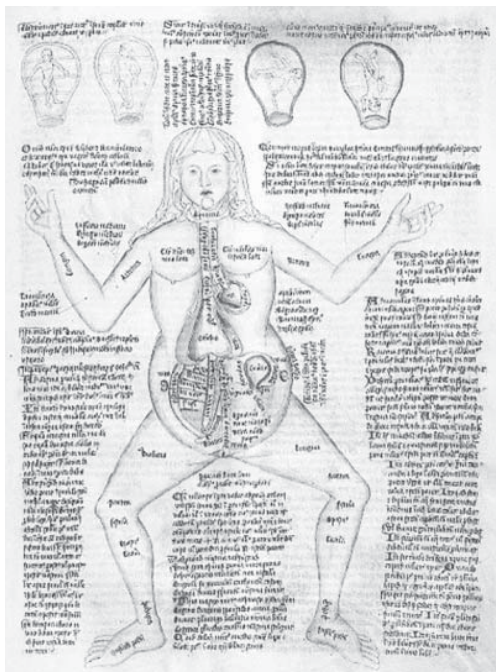
"Be fruitful, and multiply, and replenish the earth" was the command from God to Adam and Eve at the beginning of the Book of Genesis. In this context it can be understood that infertility would be a divine curse, and in a time where male infertility was unrecognized.

The Book of Genesis speaks of two sisters: Rachel and Leah. Rachel was beautiful and desired. Leah was plain and unloved. God made it possible for Leah to bear children while her sister remained childless. Despite all of her best efforts Rachel did not become pregnant for many, many years. When she finally did give birth Rachel cried out, "God has taken away my disgrace by giving me a son." This shows infertility is a taboo since times immemorial.

But the real change came with Hippocrates and his school. Born in 460 BC, Hippocrates wanted to break away from the way medicine of the time was practiced, which was closer to magic, and develop a system of medical reasoning based on rational thinking. Infertility was recognized as a medical problem which needed diagnosis and treatment and women were not subject to exclusion because of it. Hippocrates was well aware of the problems of infertility and theorized a number of causes for it and had formulated numerous treatment options.

The Egyptian Kahun Gynaecological Papyrus has several (now, unhappily, mangled) ways to "test" a woman's fertility, including experiments that involve the subject sitting on the earth covered in beer, being force-fed dates and being monitored to see if she vomited. If she somehow managed to keep it all down? Sorry, she was never going to have any kids.

During the Middle Ages, however, it was understood that procreation was a necessity and important to the "continuation of the species". If a couple's sole reason for sexual intercourse was not for procreation, their fertility would be decreased. Infertility could also be the consequence of sins committed; infidelity, and blasphemy could also give rise to infertility. Fertility might be regained with prayer and fasting. Infertility, the mark of divine punishment, was a real fear during the Middle Ages.



Women who suffered from infertility in the medieval period and Middle Ages had a hell of a time — often literally. The Malleus Maleficarum (1487) by Heinrich Kramer and James Sprenger, a vastly popular witch-hunting book from Germany, claimed that infertility could be caused by both witches and the Devil. Neither harmed the reproductive organs ... they just made them useless, poisoned the seed, or cooled the ardor between man and wife.

And if you weren't annoyed enough by people telling you to blame your womb on the Devil, childless, unmarried or widowed women were sometimes regarded as witches themselves. Deeply unhelpful!

The Renaissance marks the period of undeniable scientific progress and advancements in modern day thinking and treatment of infertility. De Graaf (1672), refuted Aristotle's theories of fertilization, and described the ovary and follicular function. Sperm was first identified under the microscope by von Leeuwenhoek in 1677. In 1752, Smellie was the first to carry out experiments and describe the fertilization process. Although progress was being made in the origins of infertility, because of a woman's apparent fragility, she automatically was at fault when the couple was infertile.

Medical authors like Philip Barrough and Rodrigo de Castro Lusitano talked freely about male infertility as well as female, and the language had become much less morally accusing, and much more medical — though perhaps not entirely accurate. Barrough, for instance, said that men wouldn't have kids if their sperm was too hot or too "cold, thin, watery and feeble," if their penises were too short ("so that they cannot cast their seed into the innermost place"), or if they had a "naughty or evil kind of diet."

The nineteenth and twentieth centuries were marked by tremendous advances in the diagnosis and treatment of infertility. In 1898, fertilization was described as the union of an egg and a sperm.

First estrogen, the female hormone, was discovered in 1923. In 1935, the male hormone testosterone was discovered. A drug called clomiphene citrate was first synthesized in 1956, and approved for clinical use in 1967. The second type was derived from the urine of menopausal women, and is therefore called human menopausal gonadotropins (hMG). It was first clinically used in 1969. These were key to the progress toward modern fertility treatments. These drugs improve the likelihood of ovulation by up to 80 percent and chances of conception by up to 40 percent.

The first human egg was fertilized in a lab in 1944 by Miriam Menkin, the news spread like wildfire; and the term "test tube baby" was coined. But for decades after the early scientific advance there was little real progress as researchers could not keep the fertilized eggs alive.

In Washington, lawmakers placed a moratorium on federal funding for IVF research, bringing progress in America to a standstill. Meanwhile, across the Atlantic, British researchers were racing toward the same goal — to successfully create the world's first test tube baby. On July 25, 1978, a healthy baby girl, Louise Brown, was born in England — the first child ever to be conceived outside the womb. Louise would later be joined by younger sister Natalie, also a test tube baby, and on May 13, 1999, just before Louise's 21st birthday, Natalie gave birth to a daughter, Casey, making her the first test tube baby to herself become a mother.

Evening News

Meet Louise, the world's first test-tube arrival

SUPERBABE

Wide-eyed Louise Brown pictured in hospital 18 hours after she was born. Today she's doing well. See Page Three

In 1981, Elizabeth Jordan Carr is born, the first in vitro baby in the US. In 1987, donor ova became available in US. In 1992, researchers in Belgium reported pregnancies using a technique to inject a single sperm cell into an egg. The procedure, known as ICSI, revolutionized the treatment of male infertility. In 1997, Atlanta infertility clinic announced first successful pregnancy in US using an egg that had been frozen.

Since those early days, a little more than 25 years ago, tremendous progress has been made in the understanding, diagnosis and successful treatment of so many of the causes of infertility. And step by slow step, infertile women have come to be considered patients in her own right, instead of a curiosity and condemned member of the human society, living in silence and misunderstanding; no longer being considered witches and burned at the stake, but replaced as the center of medical and scientific attention, and possibly lying at the very source of all human survival. Just imagine where we will be by the next 25-50 years.

Suggested Reading

- JR Thorpe. How Infertility Was Talked About Throughout History - Because To Fight A Taboo, You Need To Understand Its Origins. https://www.bustle.com/articles/76161

Proceedings of Monthly AOGD Clinical Meeting Hindu Rao Hospital, New Delhi, 30th December, 2016

Case 1

Acquired clitoromegaly: A Gynaecological Problem or an Obstetric Complication?

Mamta Gupta, Vandana Saini

Acquired non-hormonal clitoromegaly is a rare condition and is due to benign or malignant tumours and sometimes idiopathic. Few cases of clitoral abscess have been reported after female circumcision.

A 24-year-old woman was referred as a case of urethral stenosis with complaints of pain in perineal region and pain during micturition since last 4 months following LSCS. On local examination, clitoromegaly was seen, 3.5 cm X 1cm (clitoral index =350 mm) which was tender. Her total testosterone level was 24.67ng/dL, DHEA-S was 102.3mcg/dL (within normal range). USG pelvis and abdomen including adrenals was normal. Transperineal USG revealed an oblong, cystic lesion of size 3.3 cm X 1cm in clitoris with internal echoes suggestive of haematoma. She was put on analgesics. On FNAC, about 5-6cc frank thick pus was obtained. Incision and drainage of pus was done followed by marsupilization under GA . On follow up the entire swelling had disappeared.

Symptoms of UTI following delivery may not be always due to UTI. A gynecological examination is necessary to rule out traumatic sequel even if the delivery is by LSCS. Clitoral swelling if detected in post-partum period can occur due to direct obstetric trauma including the simplest of surgical intervention like urethral catheterization as in this case.

Case 2

An unusual presentation of coagulopathy in pregnancy

Deepali Garg, Sudha Salhan, Ritu Sharma, Shilpa Dhingra

A 32 year old G4A3 with 33 weeks twin pregnancy was admitted from casualty as a case of preterm labor with fever. She gave history of one episode of bleeding from gums and slight bleeding per vaginum. On examination she was normotensive and her vitals were stable, with no clinical signs suggestive of abruption, pallor was there along with generalised oedema and hyperpigmented lichenoid eruptions over lower limbs. The baseline investigations and investigations of fever were sent. The results showed moderate anaemia with severe thrombocytopenia, mildly deranged liver and kidney function tests with normal Prothrombin time. The Chikungunya IgM antibody test was positive. Blood and components were transfused. She had preterm twin vaginal delivery within 10 hours of admission with mild atonic PPH which was managed conservatively. Post delivery her condition rapidly deteriorated and she developed frank DIC and multi organ failure. By exclusion we reached to the conclusion that Chikungunya fever could be possible cause for the frank DIC in this patient resulting ultimately in mortality.

Case 3

Group A Streptococcal Necrotizing Fasciitis and Compartment Syndrome

Mala Shukla, Rekha Jain, Shweta Mishra

Following delivery of 1st Twin Vaginally on 8th September 2016 at 11:38am, and 2nd Twin by LSCS at 3:12pm for NPOL with bleeding PV, a 27 years old female developed ecchymosis on 8th POD – GAS Necrotizing Fasciitis was clinically suspected and patient was started on Tazobact, Piperacilline with Clindamycin. 12th POD – bullae and blisters with dishwater pus developed all over the vulva extending to posterior gluteal fold and over & beyond abdominal incisional site – Antibiotics were intensified. Day 15 – tense massive ascitis – discharge from wound site developed which leaked from the abdominal wound. Therapeutic tap of ascitis was done twice to relieve respiratory symptom.

Investigations showed markedly increased leucocytosis, ascitic transudate was positive for ADA. Multidisciplinary opinion of surgeon, physician & advanced critical care team of GB Pant sought. Literature search based extensive debridement from experience of necrotising fasciitis in extremities and orthopaedic cases - which was discussed and judgementally applied to this case, as during her post operative course she remained equivocal without deteriorating further.

After review and discussion with intensivists and gastroenterologists in GB Pant Hospital – anti

tuberculosis treatment (on basis of +ve ADA in ascitic fluid) along with 4 antibiotics – clindamycin, azithromycin, linezolid & gentamicin were given for 20 days. As the KFT were by 20th POD normal- signifying the compartment syndrome was not affecting MAP in the abdominal cavity.

Patient dramatically improved after adding injection Tigecycline as per culture sensitivity report on day 24. By day 29, ascitis resolved and wound improved with superficial deficit.

She was discharged and post-operative follow up 3 weeks later showed complete wound apposition. CT scan, X Ray and other investigations corroborated and reviewed for any Foreign body.

Case 4

A case report of Mallory-weiss Syndrome in pregnancy

Suman Lata Mendiratta, Rajni, Rekha, S K Mishra

Mallory- Weiss syndrome is characterized by upper GI bleeding secondary to longitudinal mucosal lacerations known as Mallory – Weiss tears at the gastro esophageal junction or gastric cardia. It may occur after any event that provokes a sudden rise in the intragastric pressure or gastric prolapse into the esophagus. It accounts for 1-15 % of cases of upper GI bleeding.

A 26 year female primigravida presented at 7 wks of pregnancy with complaint of pain in upper abdomen and throat since 1 month, associated with vomiting. Menstrual and obstetric history were unremarkable. On examination pallor and oedema were absent, PR 102/min, BP 110/70 mm Hg and systemic examination was normal. Abdomen was soft and non tender. Cervix and vagina were healthy on per speculum and uterus was AV, 6 wk size on per vaginum. Hb was 10.4 g%. Traces of albumin and sugar was present in urine along with fue ketone bodies. On USG, minimal sub chorionic bleed was found with good decidual reaction. Pt. adnexa showed a cyst of 2.5 X 2 cm.

Endoscopy findings - Linear tear at GE junction. No active bleed. Multiple erosions at GEJ. No ulcer, normal folds, Mallory - Weiss tear present but no active bleeding.

It was managed conservatively and later discharged.

All patients coming in pregnancy with hyperemesis and GI should be properly evaluated by multidisciplinary approach. Prompt diagnosis and management can give good pregnant outcome.

Tickle the Funny Bone

Compiled by Dr Nilanchali Singh
Assistant Professor, Obstetrics & Gynecology, Maulana Azad Medical College & Lok Nayak Hospital, New Delhi, India

Ayurveda's Description of Patients' Relatives

Four types of Relatives of patients,,,

1. Raja
2. Moorkh.
3. Chandaal
4. Vidur

Depending on the family we have to modify and adapt our counselling.

How to identify the Type ??

1 Raja,,,,
They give visiting card Before telling complaints.
They tell how they are connected to other doctors or VIPs

2. Moorkhs,,,
They don›t have sense of priority.
They ask about vaccination when baby is on ventilator.
They complain about mosquitoes when baby is having pulmonary hemorrhage.

3. Chandaal.
Notorious people.
They NEVER believe you.
They are sceptical about your explanation.
They ask for summary of treatment.

4. Vidur.
Majority of all other patients who suffer silently due to our frustration with other categories.
Ayurveda has given clear cut guidelines

How to deal with people.

1. Raja,,,,
Give them Respect.

2. Moorkh,,,,
Tolerate them.

3. Chandaal,,,
Give them Plan of action including Transfer to other hospital.

4. Vidur,,,,
Be honest with them.
Tell truth.
They are majority.
Treat them well.

Man: is there any medicine for long life?
Doctor: get married
Man: will it help?
Doctor: no, but it will avoid such thoughts

Answers: Crossword - Infertility

Across

2. Corifollitropin
3. Clomiphine
4. Salpingostomy
5. Uripristal
7. ERA
10. Leydig
15. Metformin
17. Teratospermia
18. Fecundability
19. Uterus

Down

1. Granu losa
6. Intralipid
8. GIFT
9. Cavernous
11. Brannstrom
12. Proliferative
13. Durga
14. Five
16. OHSS

Royal College of Obstetricians & Gynaecologists - AICC- Northern Zone India

Website: **www.aiccrcognzindia.com**

Chairperson: Dr Sohani Verma: (drsohaniverma@gmail.com / 9810116623)

Vice Chairperson	Hon. Secretary	Treasurer	Web Editor
Dr Nirmala Agarwal	Dr Ranjana Sharma	Dr Anita Kaul	Dr Arbinder Dang

ANNOUNCING NEXT COURSE

The RCOG UK MRCOG Part II Final Preparation Course Enhanced Revision Programme (ERP)

Online distance learning course (12th February – 28th May, 2017)

Limited to 15 candidates only (First Come First Serve basis)

Overview

The Enhanced Revision Programme is a 15 week revision programme organized by RCOG UK, to prepare you for the Part 2 MRCOG examination. This unique and rewarding programme is mapped to the syllabus of the membership examination and its content is developed and reviewed by experienced RCOG examiners.

Package Includes

- E-lectures live from UK. Small group tuition in a dedicated learning environment
- Virtual interactive weekly classroom sessions live direct from UK to your home
- The course will be preceded by a "Pre-Course e-Induction Module"
- Focuses on many aspects of the NHS and practice in UK, which may be unfamiliar to Indian candidates.
- Extensive revision tests with feedback from UK moderators

Important Dates

- Last date for registration **6th January, 2017**
- E-tutorials start on **23rd January, 2017** & completed by **31st January, 2017**
- Online classrooms start **12th February, 2017 - 28th May, 2017**
- **MRCOG Part 2 Revision Course (written) July, 2017 (duration 3 days-Dates to be announced later) in New Delhi -**Includes examination tips and techniques to answer exam questions, MCQs. EMQs and SAQs. (There will be separate registration formality and fees to be payable for this course at a later date)

Course Fee: Rs 35,000/- (Thirty Five Thousand Only)

UK Conveners -Dr Sanjeev Sharma

India Conveners and Contacts for details - Dr Puneet Kochhar (drpuneet.k20@gmail.com/9953001628)
- Dr Sweta Gupta (swetagupta06@yahoo.com/8130140007)

Registration Guidelines (Online registration available on website)

- **Eligibility Criteria: Atleast 70% pass marks in screening test before the online lessons.**
- Bank Transfer or Demand Draft must be made in favour of **"RCOG NZ 2012 Plus"** payable at New Delhi. (cheques not accepted).
- There will be no refunds on cancelation
- Registration request along with Demand Draft to be posted to the Secretariat mailing address as given below:-

Mailing Address: **RCOG North Zone Secretariat**
Hostel Complex- Basement, Indraprastha Apollo Hospitals, Sarita Vihar, New Delhi 110076
Tel No - 91-11-29871616/2146/2199, 09716801190/09810116623
Email: rcog_nz2012@yahoo.com/drsohaniverma@gmail.com

CELEBRATING 20 YEARS OF SERVICE EXCELLENCE

FULL SPECTRUM OF GYNAECOLOGICAL SERVICES

AT APOLLO INSTITUTES OF OBSTETRICS & GYNAECOLOGY

RANKED FIRST IN INDIA

Indraprastha Apollo Hospitals,
Voted the best hospital in North India*

*All India Critical Care Hospital Ranking Survey 2016 by The Times of India

ROUTINE & HIGH RISK OBSTETRICS BACKED UP BY OUTSTANDING

- Blood Bank • Neonatal ICU • Fetal Medicine
- Super speciality care by experts in all disciplines & ICU care
- Epidural analgesia

ROUTINE GYNAECOLOGY AND SUBSPECIALTIES

- Gynae oncology • Routine Abdominal & Vaginal Gynae Surgeries • Minimal access Surgery - Basic & Advanced Laparoscopic & Hysteroscopic Surgeries
- Robotic Surgery - Gynae & Gynaeonco Surgery
- Urogynaecology • Menopausal & adolescent Gynaecology
- Gynae Endocrinology

ASSISTED REPRODUCTION TECHNOLOGY (ART/IVF UNIT)

- Services available - OI, COS, IUI, IVF, ICSI, Semen Bank, Vitrification, Donor oocyte program and other technologies
- Full time In-House Embryologist & Lab services
- Individualized treatment for best results

FETAL MEDICINE

- Intrauterine transfusion (IUT) for fetal anemia
- Multifetal pregnancy reduction • Selective reduction in discordant anomalies • Selective reduction in monochronic twins discordant for anomaly
- Laser for twin-twin transfusion syndrome

UROGYNAECOLOGY

- Urinary incontinence: overactive bladder, stress urinary incontinence • Voiding dysfunction • Interstitial cystitis & bladder pain syndrome • Urodynamics • TOT • TVT
- Colposnopension

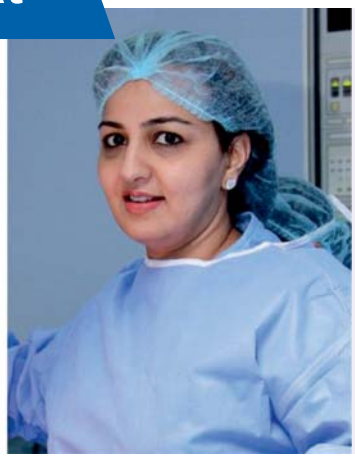
Indraprastha Apollo HOSPITALS
TOUCHING LIVES

Indraprastha Apollo Hospitals, Sarita Vihar, New Delhi - 110076 | Tel: +91-11-2987 1090 / 91 | Email: assistance@apollohospitalsdelhi.com
Follow us on: TheApolloHospitals | HospitalsApollo | apollohospitalsindia | www.apollohospdelhi.com

SUNRISE HOSPITAL
experience • expertise • care

Sunrise Hospital Congratulates Dr. Nikita Trehan

Historic Feat



Dr. Nikita Trehan recently removed a **6.5 Kg** mass from a patient's uterus that had reached up to her rib area. The excised mass is apparently one of the world's largest fibroid removed laparoscopically.

LEADING CONSULTANTS AT SUNRISE HOSPITALS

DR. HAFEEZ RAHMAN

Sr. Gynaecologist & Laparoscopic Surgeon
Leading Consultant of Sunrise Hospitals, India
International Modern Hospital, Dubai

DR. NIKITA TREHAN

Sr. Gynaecologist & Laparoscopic Surgeon
Leading Consultant of Sunrise Hospitals, India
International Modern Hospital, Dubai
(Guinness Book of World Record Holder)

DR. AJAY AGGARWAL

Gynaecologist & Laparoscopic Surgeon
Leading Consultant of Sunrise Hospitals, New Delhi

SPECIAL EXPERTISE

- Total Laparoscopic Hysterectomy, Any size of uterus(We have record for 5.4Kg TLH donelaparoscopically)
- Laparoscopic Myomectomy:
- Any size of fibroids(we have the world record for worlds largest fibroid removed laparoscopically)
- Laparoscopic & Hysteroscopic Fertility Enhancing Surgeries:
- All Hysteroscopic Procedures like Hysterescopic Myomectomy,Polypectomy,Septal Resection etc,
- Laparoscopic Oncosurgeries laparoscopic wertheims hysterectomy for CA cervix and CA endometrium laparoscopic surgeries for CA ovary.
- Laparoscopic Sling Surgery for Nulliparous Prolapse.
- All Gynae Urological Surgeries : TVT, TOT
- Laproscopic Treatment of Fistulas/ Laparoscopic Vaginoplasty by Sunrise Method.
- Specialized Vaginal Surgeries: Sacrospinous Fixation, Veginal RejuventionSurgeries
- Laparoscopic Sacrocolpopexy for Uterine Prolapse.

F-1, kalindi Colony, New Delhi-65, Tel: +91 11 4882 0000, +919810157410, E-mail: helpdesk@sunrisehopitals.in

WHITE PAPER

Every baby deserves a healthy life

Newborn Screening - A public health revolution akin to the preventive program of immunization

Newborn Screening is a preventive health measure to detect disorders not clinically visible at birth but can cause significant morbidity and mortality. The process is simple and involves a few drops of blood collected by a small lancet on a piece of filter paper. Up to 40 disorders can be tested on this sample. The test has to be performed anytime after 24 hours of birth and ideally less than 7 days after birth. A template disorder, which is the most important preventable cause of mental retardation, is Congenital Hypothyroidism.

Congenital Hypothyroidism (CH)

Congenital hypothyroidism occurs when the thyroid gland fails to develop or function. The common causes are agenesis of the thyroid gland, ectopic location of the gland and dyshormonogenesis (failure of any of the hormones to be synthesized). Mothers with hypothyroidism, when euthyroid do not cause any of the above mentioned conditions. Left undetected, it leads to intellectual disability and abnormal growth. Treatment must be started within the first 2 weeks of life of infants to prevent development of mental retardation, learning disabilities, and/or growth delays.

CH India Perspective

Globally, the incidence of CH is about 1:3000 or 1:4000. In India, preliminary research indicates that it is much higher at 1:1130.[1]

Disorder Screened	Prevalence	Effect if not screened	Effect if Screened & Managed	Management
Congenital Hypothyroidism (CH)	1:1130	Severe mental retardation, intellectual disability and abnormal growth.	Normal, if treatment begins in the first month after birth.	Daily oral dose of thyroid hormone (thyroxine)

References:

1. ICMR Multicentric Study (2007-2012)

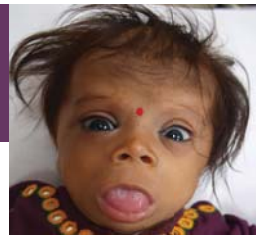
Why it is important – A Case Study

A simple blood test would have changed his life - encourage newborn screening. There is nothing more encouraging for an obstetrician to see a healthy fetus grow into an active productive child what can be better than a preventive measure right when the newborn is still under your care.

This baby Laxman now nine months old does not even hold neck and has global developmental delay. The mother is tired of his constipation. She reports that he was born healthy with good APGAR scores. The obstetrician had congratulated her on the birth of a healthy child. Somewhere something went wrong.

Her neighbour who has just been blessed with a baby daughter has undergone a heel prick test.

Baby Laxman was not screened after birth and later it was found that he is suffering from Congenital Hypothyroidism (CH). If Newborn Screening was done in time, the situation would have been in favor of this little child.



Rinki was blessed with a baby girl at the same time when Laxman was born, but she knew about Newborn Screening. After getting her baby screening, it was found that her baby is also suffering from CH. Today after 9 months, her little angel is healthy and leading a normal life.

CH prevention with Newborn Screening

This baby has congenital hypothyroidism. Imagine that a very low cost intervention in the form of supplementation of L Thyroxine could have ensured normal growth and development of this child. Let us all give our promise to encourage newborn screening.

An educational initiative by PerkinElmer

PerkinElmer® For the Better

Postal Registration No. DL©-01/1398/2016-18
January 14-15, Date of Publication, January 7-8
Registered with Registrar of Newspapers for India
DELENG/2001/04547/8.25" x 11.25"