IFS CONVERSATIONS

Volume 18

Theme

New Innovations

IFS SECRETARIAT

+91 11 40018184
+91 9899308083
+91 9667742015
indianfertilitysocietydelhi@gmail.com
www.indianfertilitysociety.org
302, 3rd Floor, Kailash Building,
26, Kasturba Gandhi Marg,
C.P. New Delhi - 110001

MESSAGE FROM THE PRESIDENT'S DESK

Dr K D Nayar
President - IFS

Dear Friends,

It is indeed a pleasure to address you all on this issue of IFS Conversations.
We look forward to seeing you all at Fertivision 2022, from 9th to 11th Dec at Hyderabad.
In this IFS conversation we have dealt with detailed new innovations. The editorial team and the authors have worked very hard towards it. Hope you all will find it very useful. The conversation also showcase various recent academic activities conducted by our extremely enthusiastic and committed member.

Wishing you all a very pleasant reading of this issue of IFS Conversation!

Dr. K D Nayar
President IFS

MESSAGE FROM THE SECRETARY DESK

Dr Surveen Ghumman
Secretary - IFS

Dear Friends,

Greetings from team IFS

IFS conversations is the official newsletter, this particular issue focuses on the innovations in the field of Reproductive medicine and infertility. Hope all members enjoy reading and keeping them professionally updated.
Please go on to the IFS website and answer the surveys we have put in for pan India data collection
We look forward to seeing you participate actively in Fertivision at Hyderabad where you would see IFS at its best – academically, socially and culturally bringing together global and national leaders in the field. Do not miss it!

Dr. Surveen Ghumman
Secretary, IFS

MESSAGE FROM THE EDITOR'S DESK

Dr Sweta Gupta
Editor - IFS

Dr Rupali Bassi Goyal
Jt. Editor - IFS

Dear Friends,

Greetings from team IFS
We are pleased to release this edition of IFS Conversations which is based on theme "New innovation"

It has collection of articles on different aspects like AI, newer concepts in imaging, genetics, OTC, Yoga and sexology. It specifically covers interviews of Lifetime awardees, President and Gen. Sec.

We sincerely thank all our authors for their wholehearted contribution towards this issue of IFS conversation.
We would love to hear your comments and suggestions and encourage all our readers to contribute in our forth-coming issues of IFS conversations..

Dr. Sweta Gupta
Editor, IFS

Dr. Rupali Bassi Goyal
Joint Editor, IFS

GOVERNING COUNCIL

Dr KD Nayar
President IFS
9810398765
kdnayar@usa.net

Dr Pankaj Talwar
President Elect
9810790063
pankaj_1310@yahoo.co.in

Dr Neena Malhotra
Sr. Vice President
9891557707
malhotraneena@yahoo.com

Dr Geeta Khanna
Vice President
9335913046
dr_khanna@yahoo.com

Dr Surveen Ghumman
Secretary General
9810475476
surveen12@gmail.com

Dr Rashmi Sharma
Joint Secretary
9810252619
drrashmisharma73@gmail.com

Dr Jayesh S Amin
Additional. Jt Secretary
9824302671
vanshvidhan35@gmail.com

Dr Shweta Mittal
Treasurer
9910303056
mshwets@hotmail.com

Dr Leena Wadhwa
Jt. Treasurer
9910933447
drleena_123@yahoo.co.in

Dr Sweta Gupta
Editor
8130140007
swetagupta06@yahoo.com

Dr Rupali Bassi Goyal
Jt. Editor
9818331760
rupalibassi@hotmail.com

Dr Nymphaea Walecha
Web Editor
9873855738
nymphaea2006@yahoo.co.in

Dr Saumya Prasad
Assistant Web Editor
saumya.87in@gmail.com

Dr Ritu Jain
Jt. Web Editor
9873183030
vmcgurgaon@gmail.com

Dr Renu Misra
Librarian
9811147217
drrenumisra@gmail.com

Dr Gaurav Majumdar
Chair Embryology
9810794610

PAST PRESIDENTS

Dr M Kochhar
Patron
9810018277 / 24352514
drmkochhar@yahoo.com

Dr M Telang
Founder President
9811030476/25822454
drmangalatelang@gmail.com

Dr Abha Majumdar
Past President
9810315807
abhamajumdar@hotmail.com

Dr Nalini Mahajan
Past President
9810087666
dr.nalinimahajan@gmail.com

Dr Kuldeep Jain
Past President
9810018951, 22443069
jainravi6@rediffmail.com

Dr Sonia Malik
Past President
9810122337
sm_doc@southendivf.com

Dr Sohani Verma
Past President
9810116623
drsohaniverma@gmail.com

Dr M Gouri Devi
Past President
9810023111

Dr Sudha Prasad
Immediate Past President
9968604341
drsprasad@yahoo.com

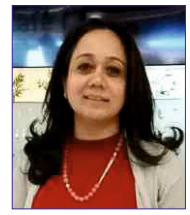
EXECUTIVE MEMBERS

Dr Sarabpreet Singh
9899009497

Dr Gaurav Kant
8750345277

Dr Pranay Ghosh
9953001858

Dr Pikee Saxena
9868223323



Dr Garima Kapoor
9810504509

Dr Parul Garg
9810428242

Dr Sabina Sanan
8860162627

Dr Reeta Mahey
9818447845

Dr Neeti Tiwari
9899470850

Dr Renu Tanwar
9968604352

Dr Puneet R. Arora
8826539305

Dr Aanchal Agarwal
9810120619

Dr Shalini Chawla
9810401471

CHAPTER SECRETARIES

Andhra Pradesh-Dr Usha Prasad
9177744546
Bihar-Dr Himanshu Roy
8002005005
Chattisgarh-Dr Prakriti Verma
9669698996
Greater Chandigarh Chapter-Dr Anupam Gupta
9855525653
Gujarat-Dr Kokila Desai
9879748760
Haryana-Dr Sonu Balhara
9811409586
Himachal Pradesh-Dr Rohini Rao
9418014312
Jammu- Dr Sandeep Kour
09419188392
Jharkhand-Dr Archana Kumari
9419226645
Karnataka-Dr Divyashree P.S
9663351451
Kashmir- Dr. Syed Sajjad Hussain
9419000077
Kerala- Dr M Venugopal
98460 70109
M.P- Dr Priya Bhave Chittawar
8109002618
Western Maharashtra-Dr Nitin Lad
9225100643
Mumbai- Dr Sayali Kale Kandari
9833879361
Nepal- Dr Rashmi Shirish
977-984-1212931
North East Chapter- Dr Mujibur Rehman
9435070660
Pondicherry- Dr Chitra T
9488818644
Punjab- Dr Sarabjeet Singh
9212607549
Rajasthan- Dr Neelam Bapna
9828037529
Tamilnadu & Chennai- Dr Rajapriya Ayyappan
7299647464
Telangana- Dr Roya Rozati
09849161421
U.P East-Dr Manjusha
98392 27478
U.P West-Dr Shashi Bala Arya
9458702305
Uttarakhand- Dr Ritu Prasad
9557120040
Vidharba- Dr Sushma
Deshmukh 9422103443
West Bengal-Dr Madhab
Chandra Das- 9836152326
Odisha -Dr Akshay Kumar
Mahapatro- 9566841306
South Tamil Nadu -
Dr Selvapriya Saravanan
94437 21809

INTERVIEW
Dr K D Nayar

Dr K D Nayar
President - IFS

Sweta Gupta: Thank you for agreeing to give us your valuable time for this interview. Members would like to know about your qualifications, experience and your journey to becoming a successful IVF specialist.

K D Nayar: I did MBBS followed by DGO & then MD in 1981 from Maulana Azad Medical College, New Delhi. Thereafter Dip. Obst from Ireland in 1997 and FICOG in 2017. I am presently working as Chief Consultant and HOD at Akanksha IVF Centre at Mata Chanan Devi hospital since 2001.

SG: Can you elaborate on your this extraordinary journey to becoming President, IFS
KD:I became President of Indian Fertility Society (IFS) in March 2022, having started as joint treasurer in 2008-2010, became Treasurer 2010-2016 , thereafter Secretary General 2016-2018 . I was elected as Sr, Vice President from 2018-20. I accepted post of President Elect in March 2020.

I am convenor of Education committee IFS 2018-2024 .I have also been actively involved in teaching as course Director of FOGSI accredited course and supervisor for IFS-Amity accredited fellowship program.

SG: How do you balance family and professional life?
KD: I am blessed with a supportive wife Dr Poonam and three children, two daughters who are now settled in US and a son who has just finished medical graduation.

SG: Members would like to know you as person. What are your hobbies or extracurricular activities?
KD: listening music and watching sports like Cricket and Gym. As a person, I am known for being very down to earth, genuine and transparent.

SG: Future vision
KD: Innovations in IVF is important and that is theme of this year's conference Fertivision.

SG: Any interesting incident u want to share in personal or professional life
KD: I still remember this young couple who presented with H/O one failed IVF Cycle done outside , where she developed OHSS. And she was very scarred to undergo next cycle . The couple were counselled and underwent another 3 cycles of IVF in our unit , taking care of previous H/O OHSS . The last frozen ET cycle she conceived and they are proud parents of twins babies . They have been visiting us regularly and as a gesture of thanks the couple has supported over the year, the whole IVF cycle of 3 needy couples. who had financial difficulty . In addition, they are still ready to support other couples in future as a gesture of gratitude.

SG: Any message to members of IFS
KD: With the introduction of ART law, there is presently a state of teething problems but with passage of time, things will be smooth, safe and well-regulated ART speciality in India.
We should continue ethical, evidence based fertility treatment to needy couples.

I would like to sincerely thank you for sparing your valuable time from your busy schedule. Your journey and thoughts are impressive and inspiring to all our members, on behalf of all, I wish you the very best for your future

INTERVIEW
Dr Surveen Ghumman

Dr Surveen Ghumman
Secretary - IFS

Educational qualification, experience, your journey to becoming a successful IVF specialist: I was always deeply interested in infertility. In the former part of my career I was associated with government hospitals where the facility for Infertility treatment could not go beyond IUI due to lack of IVF labs facilities. Hence , after afew years I became restless as I felt I could not do justice in treating those patients who needed IVF. That is when I decided to leave, get training in IVF and start in the private sector. It was a bold step to give up a secure job and build a practice from scratch. I trained at Manipal University and Cleveland Clinic USA. My training at Manipal was very intensive with excellent teachers. My experience at Cleveland made me realize that India is very much at par with countries like USA as far as IVF treatments are concerned. Over the many years that I have practiced as a fertility specialist I have come across a series of emotions - joy, disappointment, hope, despair, anger, self pity, acceptance. My mantra through the years of practice has been - Do the best for your patient and the best comes back to you

Journey to becoming Gen Sec, IFS - I joined IFS in the year it was started. With a passion for the subject since then I keenly followed the society and participated in all activities and have always held the Senior members in high esteem. I was asked to join the executive in 2008 and since then have worked for the society with passion. I remember my first assignment as a co web editor was a e bulletin where I took out the latest innovations and made it a platform to discuss legal and ethical issues. I used to research deeply for it.. Find recent dilemmas which have happened globally in the field and take the opinion of doctors in the field. Lateter as editor and then treasurer I continued to work with the same passion as I have always felt IFS to be my own society. I feel extremely proud to be associated with the society and be part of its academic ventures. It is growing with leaps and bounds and is doing relevant work in the field of academics and research. Becoming the General secretary gave me the opportunity to put some of my thoughts into action

How do you balance family and professional life? When i was younger I was a great multitasker. That skill has declined with age. Now whether it is professional or personal I take up one task at a time. But the difference is I have become very fast in completing that task. I think experience and confidence add on with age helping you to take faster decisions. But yes - I have never missed a family time or a party because I have a presentation the next day!!

Any hobbies or extracurricular activities? I do oil painting. I have been doing it since the age of 12 . My house walls are covered with my paintings. I also swim regularly and do Yoga every morning.

Future vision : Would like to be part of the change occurring to structure IVF practices in India in an ethical manner and make good research a part of each IVF centre in India. As general Secretary I would really like to put together Indian data on practices in this field and initiate indian guidelines in a proper structured manner. These small steps would make us reach a level of global excellence

Any interesting incident u want to share in personal or professional life …….. One of my first a few cases as an IVF specialist, a humbling incident- I was doing an donor egg IVF. On the day of the pickup only patients husband came to give semen as she was caught up with work. So, I passed on her prescription of progesterone to the husband and told him that she had to take daily till we do the embryo transfer. After 5 days I called her for an embryo transfer. She had perfect embryos. It was a busy day with many cases. As I did the transfer I felt all was good. An hour later as she was leaving I went over her post procedure instructions with her. I explained as usual– “Please continue progesterone ” She looked up at me and said – “Which progesterone? I am not taking anything” I was stunned. I had explained to the husband and he apparently did not communicate with her. It was difficult for me over the next afew days to not blame myself for omitting talking to patient directly. From that day on to date I never pass on instructions to the husband! Thousands of studies done on progesterone priming of uterus before embryo transfer quoted that the not just the day but even the hour when you start is important. I was now waiting for the day when I would counsel her on why the pregnancy did not happen feeling extremely guilty. She walked into my office 12 days later to share the report. I was stunned! - A positive report! Nine months later she delivered a baby girl. I have never to date quoted what happened to our scientific community because there would be disbelief. However, it remains with me, humbling me each day. A constant reminder that pregnancies don't occur because of me or because I have treated the patient well. They occur because a far stronger force is in play. The words of Paulo Coelho ring out to me “*We have to stop and be humble enough to understand that there is something called mystery”*. Each time a patient comes back to thank me I reply, “It wasn't me, it was you who did it!”

INTERVIEW

Professor Arne Sunde

Prof Arne Sunde
Norway

Historically, Nobel prizes are awarded to an individual(s) in a given subject. However, the Lifetime Achievement award recognises all the contributions made by an individual in enhancing and fostering a Society's standing in the world. One such individual, Professor Arne Sunde, a perfect friend, is honoured with a Lifetime Achievement Award by the Indian Fertility Society (IFS).
It is an honour and pleasure to listen to the lifetime journey of Arne and hear of his many contributions and achievements in the field of Reproductive Medicine, especially in Assisted Reproduction

Jayant: Dear Arne, what was your first reaction when you heard that IFS is honouring you with a Lifetime achievement award?
Arne: I was extremely humbled and surprised that IFS was honouring a Norwegian with this prestigious award in recognition of my association with the Society. I thank the Executive committee for considering me worthy of this accolade, especially Dr Kuldeep Jain, an excellent friend. I am indebted to the past presidents and secretaries of Society and membership.

Jayant: Although I have known you for more than ten years, I feel there is so much I don't know about you. Can I take you back to your birth and childhood period?
Arne: The world was waking up from World War Two's devastation and aftermath traumas, and Norway was no different. The Norwegian population was coming to terms with the realisation of building a nation without certainty of the next meal. I was born into a relatively low-income family in Trondheim, a small town, on the 16th of August 1950. My father, Asbjørn Sunde, a Civil Engineer, worked very hard to make ends meet. I was nurtured and raised by a very kind, loving mother, Brynhild Sunde, a proud housewife who ensured that we had enough food on the table. My childhood can best be described as reasonably simple growing, with a limited number of toys and other resources enjoyed by our children.

Jayant: So far, I am seeing a child who is content but hungry to know more about life. Can you share with us your educational journey?
Arne: I was seven when I joined my Primary School in 1957. It was a challenging experience as there were shortages of many items. However, as a keen swimmer, I won my first silver medal in the 1963 swimming National Championships; I continued winning silver medals at consecutive championships between 1963-1969 when I was in secondary school (1964-1966) and Gymnasium College (1966-1969).
Before joining the Norwegian University of Science and Technology (1970-1976), I spent one year in Military service, mainly in the Coastal defence section. I obtained my Master's in Chemical engineering.

Jayant: If you obtained a Master's in Chemical engineering, what motivated you to change directions towards Reproductive medicine?
Arne: Life has been challenging right from the start. I changed track mid-stream. Initially, I had planned to study computing and had written many programs for mainframe computers, or when possible, worked for the budding Norwegian oil industry. All along, I was intrigued by biochemical processes. Biochemistry teased my interest further when the legend in testis biology Kristen B Eik-Nes was appointed Professor of Biophysics. While working in the US, Eik-Nes's pioneering work reported understanding the fundamental relationship between the pituitary gland and testicular function. I decided to join him and obtained my masters under his guidance. The title of my thesis was: 'Inhibition of Testicular 5a-reductase by Progestines (1976). I was fortunate to receive a scholarship to do my PhD in Biophysics. Professor Eik.Ness, as my mentor, supported and encouraged me to complete my PhD. Thesis title: "Metabolic activation and inactivation of androgens".

Jayant: On completing your PhD, I am sure many doors would have opened for you. Can you tell our readers about your career?
Arne: In 1980, after my PhD, I started to work as an engineer and later group leader at the Institute for Cancer research. The research focus for our group was the relationship between androgens and androgen metabolism and prostate cancer. I became more administrative after a while and was heading our molecular biology laboratory (80 employees). In 1991, I went full-time into IVF. Consequently, in 1994, I was appointed Professor in Cell Biology (teaching) at the Norwegian University of Science and Technology. My main task was teaching the Biology of Reproduction to medical students. I stopped teaching in 2020
In recognition of my contributions to the state, King Harald V bestowed me with the Medal of Merits in 2017. A very prestigious royal honour.

Jayant: How did you get involved in ART?
Arne: A few gynaecologists approached me in 1982 as they wanted to start an IVF service and needed someone to analyse LH and progesterone. I was the only one at the hospital with practical experience with this analysis. As part of my PhD, I had been making radioimmunoassays of hCG from scratch (rabbit in one hand, hCG in the other and a few months later, you had an assay).

I was prepared to make our own RIA for LH and do the analysis (natural cycles), but before getting permission, we decided to go for a stimulated cycle. With six years of experience in the primary culture of testicular, prostate, and cancer cells, I was confident that I could take responsibility for the IVF culture and offered to help. We got our first IVF baby in July 1984 (first in Norway), and in 1987 the first baby was born after the cryopreservation of embryos. The IVF Unit at St Olavs university hospital has been a leading unit in Norway ever since.
I remained the laboratory manager between 1982-2006, was promoted to the Head of the Fertility Clinic in 2006, and in 2015 became the Head of the Department of Obstetrics and Gynaecology. I held this position for one year, retiring from the services in 2016—a very challenging but rewarding journey of my life.

Jayant: We all know about your association with ESHRE and all the contributions that you have made to structure what ESHRE is today. Can you elaborate on how you got associated and all the challenges you faced?
Arne: ESHRE provided a platform for me to fulfil my dreams. The birth of the first test tube baby was fresh, and many questions remained unanswered. I was one of the few Norwegian Biologists then, searching for more information to build on my existing base. It was fortuitous that I wandered into a meeting room (to pass a little time during tea break) at the third World Congress of IVF in Helsinki in 1984. There I found Robert Edwards and a bunch of keen Europeans determined to set up a society to rival the Americans. Edwards gently coerced me into ESHRE's first temporary committee, and I was given the responsibility for ESHRE's training programmes within a few months. I was the first founder executive member (1985- 1987), and in 1987, I was appointed as a Special Advisor on training (1987-1994). Eighteen years later - in 2003, I took the helm of ESHRE as its 10th Chairman. This period was challenging as ESHRE was evolving with many educational and training activities. Membership was also increasing, as was their expectation from one of the largest European Reproductive Medicine societies. The Society found itself in a far more political environment than ever before. Under my leadership, the Society formally opposed the restrictive legislation proposed in Italy (enacted in 2004). It formally supported embryo and stem cell research (which appeared under threat from EU funding and a 'rumoured' tissue and cell directive). A need for a permanent address for Society and to accommodate all the increasing activities associated with Society, I was instrumental in purchasing our own Central Office, as we know it now, in the suburbs of Brussels.

At the end of my chairmanship, I continued as the immediate past president for the next two years (2005-2007)

All the past Chairs of ESHRE and the incoming Chair met at the ESHRE meeting in Madrid in 2003.
From left to right: Pier Giorgio Crosignani, Basil Tarlatzis, Jose´ Egozcue, Lynn Fraser, Klaus Diedrich, Jean Cohen, Robert Edwards, Andre´ Van Steirteghem, (seated) Arne Sunde (Chairman-elect) and Hans Evers (outgoing chair)

Over the years, I have actively supported and influenced ESHRE members, notably in developing the Campus programmes, pre-congress courses and strategic directions. All these have been possible because of my involvement in various committees and working groups, which included:
-Working group starting work with the EU Tissue Directive (chair), Formation of the European Assisted Reproduction Consortium
-ESHRE working group on European Demography challenges (chaired the first meetings)
-Working group developing the program for Certification of Clinical Embryologist (chair)
-Working group on culture media (chair)
-ESHRE working group on Medical Devices (member)

My passion has always been to continue as a member of the culture media working group, campaigning for greater clarity in the composition of different media and aiming to produce a summary report which will empower all embryologists to improve their culture systems.

I served as the Associate Editor for Human Reproduction Update (2015-2017) and was invited to be the Chief Editor in 2019. I have enjoyed this position as it has allowed me to deliver Updates in Reproductive Medicine at the cutting edge of developmental science.

Jayant: IFS has benefited in many ways from your association. How would you describe your journey to India?

Arne: My love affair with India started in 1985. and with Kamal Buckshee. We were on our way to World IVF in Melbourne, and Kamal invited us to spend five days at AIIMS to help them start IVF. We succeeded in getting oocytes and embryos, which were transferred. Although We had no pregnancies, we had a wonderful time. This was my first exposure to India and Indian culture.
I was very excited when you approached me at a meeting in Oslo, suggesting the possibility of starting an ESHRE Preparatory course through IFS. I was happy to accept the proposal as it has been my vision to empower all embryologists from different parts of the world to be certified and have an equal understanding of the complex subject. We needed to deliver a safe practice for our patients, especially in countries with no regulations.

Indian clinics are now regulated. Kuldeep and both of us agreed that bringing structured recognition would help the authorities, and an ESHRE Certification was the way forward.

Teaching the entire curriculum in three days was a considerable challenge. However, with everyone's dedication, we have successfully conducted the ESHRE curriculum for the final exams. We all feel proud that 45 embryologists are ESHRE Certified in the tenth year. The Preparatory course has become even more popular after being delivered virtually. It is a proud moment for me to claim a success story on the eve of the tenth year because the combination of us three, You, Kuldeep and me, was/is a very fruitful combo.

We successfully introduced virtual exams, IFS being the guinea pig for ESHRE. And ESHRE, as you know, has adapted the virtual mode of examination.

Jayant: Thank you for your beautiful sentiments. As we conclude this interview, I can't stop asking you to tell us about Ingrid Brattbakk, your partner whom I met a few years ago. How would you describe her?
Arne: As you know, and I am sure you will agree, Ingrid is the most loving, kind and supportive soul. She is my pillar of strength, and nothing is difficult for her. With her by my side, I have the reassurance that I am not alone. We have six children, four from my previous marriage and two from her last marriage. We love our children and have showered upon them all our love and affection.

It has been such a pleasure and an honour interviewing Professor Arne Sunde from Norway, a recipient of the 2022 IFS Lifetime achievement award. You will all agree that he is the most deserving candidate, and he informs me that accepting this honour is not the end but a beginning of a new cycle of more visionary deliverance. Thank you, Arne, for your great friendship and support for the IFS fraternity and for establishing ESHRE as we know it now.

INTERVIEW AND MESSAGE FROM
Dr (Prof) Kuldeep Jain

Prof Kuldeep Jain
Past President , IFS

Science demands evidence, more so in the field of Human Reproduction, a fast-evolving arena, especially in a country, which has seen an explosion of Assisted Reproductive Technology with no regulatory controls until recently.
The lifetime achievement award recognises an individual who shines like a torch, setting and establishing pathways and examples for the rest of the fraternity to embrace the safe deliverance of sound treatment options.
One individual whom the Indian Fertility Society is proud to honour and bestow a Lifetime achievement award is none other than our own Dr (Prof) Kuldeep Jain.

Sweta Gupta (SG): Sir, many congratulations on being nominated for the Lifetime Achievement award. What was your first reaction to this news?
Dr Kuldeep Jain (KJ): I was humbled that the present IFS leadership and nomination committee appreciated my efforts in developing and nurturing the growth of IFS over last 17 years , and I acknowledge their love and affection in the form of a Lifetime achievement award. Accepting this award does not mean the end of my efforts or contributions to the mission and Vision of IFS . In fact I am having lot of plan for IFS in coming years and working on lots of international collaborations and I seek support of all my colleagues in my future endeavours.

SG: Sir, members would like to know about you as an individual, your likes and dislikes?
K J: I was born in Jaswant Nagar, a small town in Uttar Pradesh, on the 10th of September 1959. Ours was a business family, and I am the youngest of three brothers. I was my parents' favourite, who loved spoiling me, and I enjoyed being pampered. My childhood was a happy, fun-loving, carefree period without any worries or concerns, which I cherish very much. School days were filled with mischief like any other child going through the same realisation of life.

S G: Sir as a brilliant scholar, we would like your reflection on your educational journey and your interest in Infertility.
K J: I received my early education from Etawah UP and Gwalior. I graduated from S S Medical College Rewa with a gold medal in anatomy, Pathology and PSM in 1982 and was awarded an MD in Obstetrics and Gynaecology in 1986. During my MD training, I became interested in infertility and reproductive medicine. My boss Professor S C Saxena motivated and nurtured my desire to understand the field of infertility .In those days , it was all clinical as even ultrasound was not available in my college as it was only available in bigger institutions like AIIMS .The interest further grew with the time spent with Professor B N Chakraborty in 1994, whom we all respectfully called the father of ART, who mentored and inspired me in ART techniques. I recall my debates and discussions with the Professor and how he would prompt me to ask questions about every small aspect of ART. This lead to my fellowship in reproductive medicine at KKIVF , KK Hospital , Singapore where I learned the tricks of ART and sharpened my skills in both clinical and embryology , thx to Balaji Prasath , head of embryology at KK IVF who really mentored my skills in embryology and became a very good friend over the years .

S G: You your self have been an avid teacher and educationist throughout. Can you elaborate on your clinical journey and passion in teaching and education?
K J: I joined Nanavati Hospital Mumbai in 1987 as a registrar and joined UCMS as a senior resident when I returned to Delhi. I have been passionate about teaching and even as a child I was a very good debater. Because of this passion for teaching, I opted to continue and join the teaching cadre at the University College of Medical Sciences, Delhi University and continued as a Reader till 2000. Later Joined as professor at Mujaffarnagar medical college . During this long period of 14 yrs , I was involved in lot of research activity in infertility , teaching post graduates , nurturing them for thee future journey . The whole experience was highly gratifying though a bit challenging because of limited resources available.

S G: When did you treat your first infertile couple? and was there any struggle in establishing yourself as a successful ART consultant.
K J: My first independent infertility patient was as early as during my PG days when I got my ist pregnancy with clomiphene citrate. It was a real wonderful feeling I can't express in words. When I joined UCMS, Scenerio was very different, you had to arrange everything for your patients if you want to do something different. I had to fight to get a place for setting up my IUI lab, which was the first IUI lab in the government sector in Delhi. In the government sector, Infertility treatments were in its embryonic stage, and even I had to prepare my media in haematology lab (though unofficially) as the readymade media was not available. and I had to struggled for the next eight years to realise my dream of establishing an IVF facility in the government sector but unfortunately failed because lack of any support . As a fighter, I was not prepared to accept defeat and decided to start my own IVF practice. It was a very hard decision for me as I was due for my promotion to professor post shortly, and there was hardly any support from outside. Initial two years were full of struggle to establish myself but finally it has been rewarding and highly satisfying and successful journey so far.

S G: Sir, we all are aware that you are an important pillar of Indian Fertility Society (IFS) and your contribution to growth of IFS are well known. Will like to know more for the benefit for our readers, the reasons for establishing IFS?
K J: In 2000, the ART fraternity in India was still struggling as a lack of scientific dialogue, sharing of knowledge and proper guidance within the fraternity. Moreover, there were not any opportunity for training in the field. This lack frustrated me very much; as I am sure, it did others. Soon I realised that there was a need for a platform to facilitate the needs of many Infertility specialist in North and other parts of India. I kept on thinking on such a possibility for almost two years until I got an opportunity to realise this dream. I clearly remember that it was a conference in Mumbai when I got an opportunity to discuss this proposal with four colleagues from Delhi, Dr Mangalam Telang , Dr SN Basu Dr Raj Chakravarty and fortunately they were very positive but slight hesitant but finally proposal was instantly accepted and that was the start of process of a new chapter in the history of ART in India . The seed for IFS was shown. On returning back, it took me almost 2 months to convince other colleagues and to organise a meeting which was called at Delhi gymkhana club and 18 members joined that historic meeting . The proposal to launch Indian fertility society was passed by a voice vote. And we established a fertility platform, IFS with 18 founder members, in 2005. As a founder secretary, I had an opportunity to steer the development of the society to embrace the needs of the members, for open communication, newer developments, experiences and difficulties. Initial years were very challenging as a very big task was in hand to bring people with different aspirations under one umbrella for a common goal , Had to write the constitution keeping in mind everyone's interest , giving the society a pan India character. I remained the founder secretary, steering a successful path till 2008, then as a Vice President and later as the President of the society from 2011 – 2014

S G: Sir, we have all witnessed your passion for teaching and education and collaborations with international bodies, can you share your vision?
K J: As a scholar, I believe in sharing the knowledge with all those who are willing to accept it. I became instrumental in developing and introducing academic programmes in clinical and Embryology arenas. I was successful in establishing an affiliation with Amity University with the help of Dr Sohani Verma, running of IUI workshops across India, and ten years ago introduced the preparatory course in Embryology for ESHRE EXAMS and IFS certification for Embryologist. This has become the most successful programme helping and empowering many budding embryologists in India in achieving a worldwide-recognised Certificate. This was only possible because of unconditional support and help from friends like Dr Jayant Mehta and Professor Arne Sunden.
ESHRE recognised the need for an online exam for its certification course and, in 2019, for the first time, IFS held virtual exams for candidates in India outside Europe. The concept of the online exams has been adopted by ESHRE for candidates worldwide later.
I was further responsible for conceiving and introducing the official Journal of IFS 'Fertility Science and Research. I have developed international ties and collaborations with ESHRE, IFFS and ASRM. All these were possible because of widespread support from all subsequent IFS leadership and IFS colleagues across India. My efforts in establishing stronger links with International Societies bore fruits when in 2017, IFS organised the first joint IFS and ESHRE campus workshop on Endometrium in Delhi.
An MOU signed between IFS and ESHRE / ISAR further solidified the association and started a joint IFS/ISAR session during ESHRE annual conference. An extension of this association was the deliverance of a highly successful virtual FUSION 2022 Conference, a collaboration between ESHRE-IFS and ISAR. This is now an established feature till 2026.
As an organising secretary, in 2016, India witnessed the first IFFS world conference, which was a huge success and gave India its due share after 55 years and this was possible because of the collaboration started at 2010 with IFFS when the conference was jointly awarded to IFS and ISAR . An MOU was signed for continued cooperation between IFFS and IFS. Representing IFS, I was invited to be a member standard and practice committee from 2014-2016, one of the board of directors from 2016-2019, and nominated as member scientific committee 2019- 2025. IFS has established exchange sessions and panel discussions at IFFS 2019 Shanghai and Athens 2023.
As International committee chairperson IFS, I am continuously working to strengthen ties with ASRM, the British Fertility Society, to name a few and sincerely hope that IFS will be having its write place soon at international scene .

Nationally, I have contributed and given directions to academic activities and growth q was of the East Delhi Gynaecologist forum as Vice President and later as President. I have also established long associations with AOGD as an executive member and chairperson of the infertility committee of AOGD. At the FOGSI's level my role as a member of the infertility committee and a member of the international exchange committee was very fruitful. Recently as a chairperson of the endometriosis committee has given me an opportunity to contribute immensely to FOGSI, allowed me to bring out a FOGSI focus and awareness program on adolescent endometriosis across schools in India.

S G: Sir, we have learned a lot about your academic contributions, but members will like to know who the person behind your success is.
K J: As is the tradition in Indian families, as I was evolving and establishing my self in my clinical and academic career, my parents felt it was time to for me to get married. They found an excellent match in Dr Bharti, and we got married in 1987. We are blessed with a daughter and son. Mannsi, has followed my example, supports me in our daily clinical practice, and already had been sharing lot of my responsibilities. On the other hand, Bharti as a specialist ultrasonologist, continues to support me always in my day-to-day clinical and social activities. I am very proud to have a very understanding and loving family and whole credit goes to my family who have allowed me to pursue my dreams inspite of hardships at times.

SG : You are being followed by a large no of young budding clinicians and embryologist any massage or advice to them.
KJ : there is a tendency in lot of youngsters to take shortcuts to achieve their goals . There are no shortcuts and no substitute for hard work. My advice to them is work hard, be focused, practice ethically, observe all new laws in force and keep yourself updated

SG : Last question , what are your hobbies and what do you do in your free time .
KJ : I am a foodie and cooking is my stress buster and I consider myself a good cook . Apart from that I am a social person and love to be with friends, enjoy travelling and do some singing (though were always hooted in my college days).

Sweta Gupta: It has been such a pleasure interviewing an eminent clinician and an academician. Someone who has vison to enrich and empower all the fraternity with the advances in science by providing them with evidence. I for sure am convinced that with the blessing of scholars like Dr Kuldeep Jain, we the younger upcoming fraternity will continue to enjoy the fruits of his efforts. Thank you very much sir for such an elaborate and detailed interview. We wait to applaud you on the stage as you receive your Lifetime Achievement Award.

INVITED
ARTICLES

Ovarian Tissue Cryopreservation and It's Eventual Transplantation: Is It Proficient Fertility Preservation Programme?

Authors: -

Dr. Prof (Col.) Pankaj Talwar, VSM

Director, Medical Services, Birla Fertility & IVF
Director, BFI
M: 9810790063
Email: pankaj_1310@yahoo.co.in

In current times, there has been a constant need for evolution of cryopreservation techniques to assist women and adolescent girls facing urgent prerequisite for treatment of cancer and simultaneously aid in their fertility preservation (FP) for maintaining their active and efficient future reproductive status. Ovarian Tissue Cryopreservation (OTC), also known as ovarian cortex freezing, is considered one of the best suited option that has gained substantial recognition as experimental tag has been removed from it recently in the year 2019. This section of the reproductive age group woman and adolescent girls suffering from various types of cancer may experience impaired fertility or hormone production as a result of their exposure to gonadotoxic chemo-radio therapy prior to or during the course of combating cancer [1,2,3]. The main objective is the maintenance of the ovarian structure, physiology and endocrinology, benefiting multiple target patients facing different treatment and medical management situations. Moreover, OTC is the only fertility preservation alternative for prepubertal patients, since in these cases, as neither the ovarian stimulation protocols nor oocyte collection can be applied [4].OTC encompasses re-implantation of a few thawed cortical strips into the patient (i.e., auto transplantation) once the patient has completed cancer treatment, is disease free, and desires pregnancy. The number of live births after ovarian tissue cryopreservation exceeded 200 in 2020 [5], while the pregnancy and live birth rates reached 50 and 41%, respectively [6]. Though live births have also been reported by heterotopic transplantation [7, 8], the exact numbers are still unclear.

Concerted multidisciplinary discussions between Hematologists, Assisted Reproductive Technology (ART) teams and Surgeons are required to improve the quality of patient information [9] in terms of procedures and measures for achieving OTC successfully. Radio sensitivity of the human ovary that leads to the loss of 50% of primordial follicles (LD50) is estimated to be 2 Gy [10, 11, 12]. The possibility of ovarian failure is also determined by the regimen and type of chemotherapy where block of DNA replication, double stranded (ds) DNA breaks, and induction of apoptosis primarily in the stroma and the granulosa cells of growing follicles occur[13, 14].

Studies investigating the most favourable cooling rates and dehydration times have been conducted. It is now well established that for obtaining satisfactory results, adequate penetration of cryo-protectant through the stroma and granulosa cells to the oocytes is required [15]. However, when compared to vitrification, very few reports of successful births were reported in comparison to implementing the slow freezing method for OTC based FP. Although OTC is expected to bridge an important gap in FP in the field of onco-fertility in cases where it is impossible to create embryos for cryopreservation, especially in paediatric oncology mostly among young girls prior to adolescence [16, 17].

OTC comes with four key components that involve: (i) ovarian surgical procurement, (ii) ovarian tissue processing, (iii) tissue cryopreservation, and (iv) Storage followed by ovarian tissue transplantation (OTT). We as an expert are not only suggesting and recommending OTC as FP method that is being applied to benefit cancer patients, but also the women who want to postpone their fertility and menopause can opt OTC [18].

It was in 2006 when Meirow et al. reported the first live birth obtained from OTC [19]. However, claims of the first live human birth coming from ovarian tissue which was cryopreserved using the slow freeze technique and then transplanted was described by Donnez et al. [20].

OTC in turner syndrome is under investigation but there is no published report showing any success in such cases [21]. Though, the cryopreservation and re-implantation of whole ovaries are areas where extensive research needs to be performed prior to offering such high-end medical service to the necessitous, in future.

The present stance of OTC is hopeful for young cancer sufferer females and future perspective of OTC/OTT seems to be promising enough, to help the society specially cancer victims. The long term associated and unseen risks of metastasis in young female patients with malignancies who had ovarian cortex re-implanted is still a matter of research and concern and needs to be explored. Nevertheless, optimization of both, cryopreservation strategies and thawing/warming protocols is the need of the hour and necessary to improve the survival of follicles in cryopreserved ovarian cortex.

REFERENCES

[1]. DeSantis CE, Lin CC, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2014. CA:Cancer J Clin. 2014; 64(4):252-71.

[2]. International Agency for Research on Cancer [Internet]. Lyon: Cancer today [cited 2018 Dec 7].

[3]. Gosden RG, Baird DT, Wade JC, et al.Restoration of fertility to oophorectomized sheep by ovarian autografts stored at -196 degrees C. Hum Reprod. 1994; 9(4):597-603.

[4]. Donnez J. Fertility preservation in women, focusing on cancer, benign diseases and social reasons. Minerva Ginecol. 2018 Aug; 70(4):385-6.

[5]. Dolmans, M.M.; Falcone, T.; Patrizio, P. Importance of patient selection to analyze in vitro fertilization outcome with transplanted cryopreserved ovarian tissue. Fertil. Steril. 2020, 114, 279–280.

[6]. Shapira, M.; Dolmans, M.M.; Silber, S.; Meirow, D. Evaluation of ovarian tissue transplantation: Results from three clinical centers. Fertil. Steril. 2020, 114, 388–397.

[7]. Stern CJ, Gook D, Hale LG, et al. First reported clinical pregnancy following heterotopic grafting of cryopreserved ovarian tissue in a woman after a bilateral oophorectomy. Hum Reprod. 2009; 24(7):1670-83.

[8]. Oktay K, Buyuk E, Veeck L, et al. Embryo development after heterotopic transplantation of cryopreserved ovarian tissue. Lancet. 2004; 363(9412):837-40.

[9]. Mancini J, Rey D, Preau M, et al. Infertility induced by cancer treatment: inappropriate or no information provided to majority of French survivors of cancer. Fertil Steril.2008;90(5):1616-25.

[10]. Wallace WH, Thomson AB, Kelsey TW. The radio sensitivity of the human oocyte. Hum Reprod. 2003;18:117-21.

[11]. Wallace WH, Thomson AB, Saran F, et al. Predicting age of ovarian failure after radiation to a field that includes the ovaries. Int J Radiat Oncol Biol Phys. 2005; 62:738-44.

[12]. Meirow D, Biederman H, Anderson RA, et al. Toxicity of chemotherapy and radiation on female reproduction. Clin Obstet Gynecol. 2010; 53:727-39.

[13]. Lopes F, Smith R, Anderson RA, et al. Docetaxel induces moderate ovarian toxicity in mice, primarily affecting granulosa cells of early growing follicles. Mol Hum Reprod.2014; 20:948-59.

[14]. Roti Roti EC, Leisman SK, Abbott DH, et al. Acute doxorubicin insult in the mouse ovary is cell- and follicle-type dependent. PLoS One.2012; 7:e42293.

[15]. Hovatta O. Methods of cryopreservation of human ovarian tissue. Reprod Biomed Online. 2005; 10:729–34.

[16]. Jadoul P, Dolmans MM and Donnez J. Fertility preservation in girls during childhood: it is feasible, efficient and safe and to whom should it be proposed. Hum Reprod Update. 2010; 16: 617-630.

[17]. Practice Committee of American Society for Reproductive Medicine. Ovarian tissue cryopreservation: a committee opinion. Fertil Steril. 2014; 101:1237-1243.

[18]. Kim S, Lee Y, Lee S, et al. Ovarian Tissue Cryopreservation and Transplantation in Patients With Cancer. Obstetrics Gynecol Sciences. 2018; 61(4):431.

[19]. Meirow D, Levron J, Eldar-Geva T, et al. Pregnancy after transplantation of cryopreserved ovarian tissue in a patient with ovarian failure after chemotherapy. N Engl J Med. 2005; 353(3):318–21.

[20]. Donnez, P.J.; Dolmans, M.M.; Demylle, D.; Jadoul, P.; Pirard, C.; Squifflet, J.; Martinez-Madrid, B.; Langendonckt, A.V. Livebirth after orthotopic transplantation of cryopreserved ovarian tissue. Lancet 2004, 364, 1405–1410

[21]. Ye M, Yeh J, Kosteria I, et al. Progress in Fertility Preservation Strategies in Turner Syndrome. Front Med (Lausanne). 2020 Jan 24; 7:3.

INVITED
ARTICLES

Incidence, Prevalence and Epidemiological Aspects of Endometriosis

Corresponding Author: -
Dr. Roya Rozati
MD(A.I.I.M.S,Delhi),F.R.C.O.G.(London),
Professor and Head,Dept of Obst &Gynecology, Shadan Institute of Medical Sciences
Member Secretary,
Maternal Health and Research Trust(MHRT), Banjara Hills,Hyderabad-34,
India.
Tel: 9849161421 | Email: drroyarozati@gmail.com

Declaration: The article was not published or under consideration, in part or whole, simultaneously in any other journal or proceedings.

Abstract:

Endometriosis is a complex, inflammatory disease which affects more than 190 million women globally and upto 10% of women of reproductive age. It is one of the common causes of chronic pelvic pain in women of reproductive age and associated with infertility. Endometriosis affects significantly the quality of life of women, in all its aspects including sexual life, work, and social relationships. The affected area in endometriosis is the pelvis. The causes of infertility in women with endometriosis may range due to anatomical distortions, adhesions, fibrosis to endocrine abnormalities, and immunological disturbances. It is a complex interplay between the genetic profile, hormonal activity, menstrual cyclicity, inflammation status, and immunological factors that defines the phenotypic presentation of endometriosis. To date, imaging techniques, laparoscopy represent the gold standard in diagnosing endometriosis, of which transvaginal ultrasonography and magnetic resonance imaging bring the most value to the diagnostic step.

Introduction:

Endometriosis is a chronic debilitating disease with features of chronic inflammation. It appears to be one of the most common benign gynaecological proliferations in premenopausal women since it is estimated that 10-15% of reproductive-aged women suffer from endometriosis, (1) and 70% of women with chronic pelvic pain (2). Worldwide, 247 million women are reported to suffer from endometriosis, and around 47million in India are reported to have endometriosis. The usual location of endometriosis is in the pelvis. However, endometriosis has been described in extrapelvic sites, including anterior abdominal wall, surgical scars, diaphragm, omentum, small intestine, appendix, lung, urinary tract, musculoskeletal, and neural systems. The biology of endometriosis is unclear. Due to its exact prevalence is unknown, because surgery is required for its diagnosis, this disease remains poorly understood.

Due to the invasive properties of endometrial cells in patients with endometriosis, it behaves as cancer, but it is not cancer. Therefore, it gets implanted in other sites other than pelvic organs including the caesarean scar, subcutaneous tissue, cervical region. Genetic predisposition,

superimposed by hyperestrogenic stage in women will be the most important etiological factor in patients with Endometriosis.

The etiology of endometriosis remains unclear. Different theories apart from the genetic, familial, environmental pollution, Coelomic metaplasia theory, Sampson theory has been postulated earlier.

Incidence and Prevalence of Endometriosis

The Estimates of the frequency of endometriosis vary widely, but the prevalence of endometriosis in general estimated to be in around 10-15% of the women of the reproductive age group.

Worldwide it is reported more than 247 million (3) women are reported to suffer from endometriosis, and around 42 million in India(4), 2 million in UK (5) are reported to have endometriosis and the average age is around 18-35 years. In some cases, endometriosis may have subclinical course; therefore, the real prevalence seems to be underestimated. The incidence in infertile women ranges from 30% to 50%(6).Several research studies conducted in the Indian population have shown the incidence of endometriosis to range from 34% to 48% as diagnosed by laparoscopy.(7,8)The disease is associated with chronic pelvic pain (40%-50%), dysmenorrhea (60%-80%), dyspareunia (40%-50%), and subfertility (30%-50%)(9,10).Unfortunately, for many of

these women, there is often a delay in diagnosis of endometriosis resulting in unnecessary suffering and reduced quality of life. In the general female population, assessing the rates of endometriosis is immensely challenging to quantitate because the definitive diagnosis requires surgical visualization (11).

Based on the Prevalence it is reported about 10-15% of women have some degrees of this disease respectively and approximately 2% for undiagnosed symptomatic disease(12), 1/3rd of women have chronic pelvic pain with visualized endometriosis. Concerning women with pain or infertility, the prevalence of subtle, typical, cystic ovarian and deep endometriosis was reported in over 80%, 50%, 25%, and 15% of cases,

It is reported that around 42 million women are estimated to be suffering from endometriosis in India and the average age is around 18-35 years. Endometriosis is a relatively common disease, with an estimated prevalence among women of reproduction age of women of 10%. More than 20% of women are often asymptomatic and should not undergo abdominal exploration or biopsy

procedures. An accurate diagnosis requires the direct visualization of the pelvis during a thorough laparoscopic surgical observation. Based on current knowledge, up to 50% of women referred for fertility problems, 2–5% of postmenopausal cases, and 10–70% of patients with pelvic pain are linked to endometriosis. Endometriosis is usually clinically manifested with chronic pelvic pain, dysmenorrhea, dyspareunia, and subfertility (13,14,15). Due to miss treatments, it takes an average of 7-10 years to get diagnosed in most women, and a general lack of awareness about the illness itself contributes. Few Research studies investigated endometriosis incidence and prevalence among adolescents of visually confirmed endometriosis among adolescents with pelvic pain ranges from 25% to 100%, with an average of 49% among adolescents with chronic pelvic pain and 75% among adolescents unresponsive to medical treatment.(16) In Australian study reported 11.4%(17) in reproductive women.

Classification of Endometriosis:

Currently, the definitive method to diagnose and stage endometriosis and evaluate the recurrence of disease after treatment is visualization at surgery(18).It is associated with pain symptoms that have been established by the American Society for Reproductive Medicine (19).based on the morphology of peritoneal and pelvic implants such as red, white, and black lesions, percentage of involvement of every lesion should be included. The revised scoring system of the American Society for Reproductive Medicine is used to determine the disease stage. Stages of endometriosis consistent with ASRM guidelines are stage I, II, III, and IV determined supported the purpose scores and correspond to minimal, mild, moderate, and severe endometriosis. It is based on the type, location, appearance, and depth of invasion of the lesions and therefore extent of disease and adhesions.

Endometriosis fertility index is a simple robust validated clinical tool that predicts Pregnancy rates for patients after the surgical staging of endometriosis

Nonsurgical diagnostic approaches like transvaginal ultrasonography and magnetic resonance imaging (MRI) perform within the detection of peritoneal and ovarian implants and adhesions.

All of these classifications divide endometriosis into four stages related to the increasing severity of the ovarian lesions, particularly the number of endometrial implants, their depth, size, and adhesions. Points are tallied on a form and a stage is assigned based on the number of points. Scoring of Stage I (Minimal)-1-5 cm, Stage II(Mild)- 6-15, Stage III (Moderate)-16-40, Stage IV

(Severe)>40 indicates severe condition with many deep implants, large cysts on one or both ovaries with dense adhesions (20). But the correlation between lesions and pain symptoms or infertility is unclear. It is assumed that 70%–80% of lesions are stable or progress, thus endometriosis is considered a recurrent chronic disease requiring long-term management.

Diagnosis of Endometriosis

Endometriosis can be difficult to diagnose, with some studies showing an average delay in diagnosis by 7-10 years,(22) resulting in decreased quality of life and disease progression. The operative laparoscopy compared with laparotomy represents the gold standard method for the detection of endometriotic implants under magnification in the pelvis. The women who undergo laparoscopy for a definitive diagnosis due to pain symptoms may differ in pathophysiology, symptomatology, and risk factor profiles. The disease severity is assessed by simply describing the findings at the surgery or quantitatively using American society of Reproductive medicine and Histological findings need to be confirmed. Visualization of areas of endometriosis may be followed by excision or destruction by burning. This can be done simply with the diathermy or using the laser (23). History and physical examination are based on cyclic or chronic pelvic pain, dysmenorrhea, dyspareunia, a fixed retroverted uterus, an adnexal mass, uterosacral ligament.

Ultrasound examination establishes a presumptive diagnosis of an ovarian endometrioma but cannot reliably peritoneal implants of the image. Other methods of diagnosis include Non-Invasive

–Therapeutic Imaging –Ultrasound, MRI, Endometrial nerve fibers, CA 125, and others.

Epidemiology:

Epidemiology of endometriosis is important as endometriosis is a major cause of infertility and pelvic pain in many women(24). As there is no currently no non-invasive, reliable methods for the diagnosis of Endometriosis, and the true prevalence of Endometriosis is not known At Present Laparoscopy is considered as gold standard for the operation of choice for the Diagnosis of Endometriosis which is better than laparotomy for minimal to mild stage of endometriosis, which is evaluated thoroughly in asymptomatic patients during tubal sterilization.

The rates of endometriosis in the general population are difficult to quantify because the definitive diagnosis requires surgical visualization. The epidemiology of infertility depends on the geographic region, patient's age or other comorbidities and ranges from 3.5% to 16.7% in developed countries (25). It is a significant problem in women's health because of the associated suffering, the many surgeries, and therefore the health care expenses, along with the suggested link with pollution and with many problems such as cardiovascular disease. Understanding the disease might help to improve treatment and develop prevention strategies. The accurate assessment of the endometriosis burden requires detailed information related to its occurrence and incidences in the general population.

The complexity of the pathogenesis and therefore the pathophysiology of this disease is the reason for the existence of varied controversies as regards the optimal effective treatment modality for endometriosis. The purpose of surgical management should specialize in the confirmation of pre-operative diagnosis, the exclusion of malignant transformation, the relief of chronic pelvic pain, dysmenorrhea, dyspareunia, or dyschezia, and the preservation of future fertility (26). The disease has an increased rate of recurrence after bilateral oophorectomy

Surgery for endometriosis and endometrioma is often performed by laparotomy or laparoscopy, as both techniques end in similar symptom regression, fertility treatment, cyst recurrence, and major complication rates.

The operative laparoscopy compared with laparotomy represents the gold standard method for the detection of endometriotic implants under magnification within the pelvis. The laparoscopic approach offers lower morbidity, minor post-operative adhesions, and lower duration of hospitalization with a significantly better aesthetic result.

An association of endometriosis, immune dysfunction, and common obstetric and gynaecologic diseases (27).

Risk Factors and Etiology of Endometriosis:

Several reproductive factors are associated with the development of endometriosis include conditions that increase the chances of retrograde menstruation and genetic/hereditary

factorssuggesting hormonal variation may have a significant impact on the risk of developing endometriosis

Risk factors for endometriosis include infertility, early menarche, Nulliparity, dysfunctional uterine bleeding, aberrant estrogen levels, low body mass index, long duration of menstrual flow, heavy bleeding during menses, and shorter cycles, Environmental toxicants like diethylstilbesterol, polychlorinated biphenyl exposure, diet high in fat, red meat and prior surgeries or medical therapy for Endometriosis.(28,29)Regular exercise of >4 hours/week, higher parity, and longer duration of lactation were all associated with a decreased risk for endometriosis.

Pathogenesis:

The cause of endometriosis is complex, and the leading theories include retrograde menstruation with the transport of endometrial cells, metaplasia of coelomic epithelium, hematogenous or lymphatic spread, and direct transplantation of endometrial cells. A combination of these theories may be likely to be responsible.

Endometriosis may occur when the deficiency in Genetics influences, bimolecular aberrations in eutopic endometrium, dysfunctional immune response, anatomical distortions, and proinflammatory peritoneal environment may be ultimately involved

The 3 Distinct entities involved are Peritoneal, Ovarian and Deeply Fibrotic.

Clinical Management of Endometriosis:

Clinical suspicion of endometriosis usually is a product of the history and physical examination. Confirmation of endometriosis, however, requires direct visualization and occasionally biopsy if the surgeon is uncertain of the diagnosis. The initial clinical assessment identifies patients at risk for endometriosis who should undergo further evaluation by laboratory tests, diagnostic imaging, and laparoscopy.

Laparoscopy is the gold standard for the diagnosis of endometriosis(31,32). Because of the heterogeneous and sometimes subtle appearance of implants, however, the accuracy of diagnosis depends on the ability of the surgeon to identify the disease. Endometriosis may be found anywhere in the abdominal and pelvic cavities. A thorough and systematic examination of the pelvis and abdomen is essential in all patients to identify Imaging studies may be a useful adjunct in the identification of patients with endometriosis. Among the various techniques available, ultrasonography and magnetic resonance imaging (MRI) are the most useful. Techniques such as standard radiography and computed tomography are rarely useful in the diagnosis of endometriosis.

Imaging studies may be a useful adjunct in the identification of patients with endometriosis. Among the various techniques available, ultrasonography and magnetic resonance imaging (MRI) are the most useful. Techniques such as standard radiography and computed tomography are rarely useful in the diagnosis of endometriosis. Ultrasound examination is primarily used to detect endometriosis. The usefulness of ultrasonography in detecting focal implants is poor with a reported sensitivity of as low, whereas the sensitivity and specificity in relation to the detection of endometriomas and endometriosis is 83% and 98% respectively. The diagnostic accuracy can be improved by Doppler flow studies. A scoring system based on clinical parameters, CA-125 levels, ultrasound findings, and Colour Doppler flow had a sensitivity and specificity above 99% MRI is a superior method in the detection of endometrioma and is useful when further characterization of the adnexa is required. The diagnostic sensitivity, specificity, and predictive accuracy for MRI diagnosis of endometriomas are 90%, 98%, and 96%, respectively, and can be useful in monitoring therapeutic response to treatment of endometriomas.

Laboratory Tests:

Serum CA-125 levels have been assessed in several studies as a diagnostic test for the detection of endometriosis. Although elevations in CA-125 concentration have been associated with endometriosis, the performance of CA-125 testing as a reliable screening test for endometriosis has been poor because of low sensitivity in detecting the disease

Treatment:

The management of endometriosis requires a multidisciplinary approach with

[i] Surgical diagnosis and debulking of disease load

[ii] Hormonal treatment to suppress and delay recurrence and progression of the disease,

[iii] Pain management strategies best provided by a pain centre clinic that develops individualized care plans and pelvic therapy. Symptomatic endometriosis is usually treated by surgical or medical treatment both equally effective. Despite the availability of treatments of associated pain, recurrence of endometriosis isn't uncommon. The selection of medical treatments is done based on side effect profile, cost, and personal preference. Non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose combined oral contraceptive pills (COCPs) such as ethyl Estradiol and progestins are the first-choice drugs.

Surgical techniques include excision or removal of endometrial implants, ablation of uterosacral nerves by the employment of endocoagulation, electrocautery or laser treatment, presacral neurectomy, and hysterectomy with bilateral salpingo-oophorectomy. They have a 50%–80% success rate in reducing symptoms. Unfortunately, endometriosis recurs in 5% to 15% of cases even after hysterectomy and bilateral oophorectomy. The first advantage of the surgery for infertility related to endometriosis is to enhance the probability of natural conception (33). Surgery for infertility or pain increases the spontaneous postoperative pregnancy rate (34). On the other hand, surgery for endometrioma could lead to reduced ovarian function and therefore the possible loss of the ovary. Therefore, the choice of surgery should be made carefully, particularly in women with advanced age, bilateral disease, impaired ovarian reserve, who had previous surgery for endometriomas, or long-term infertility, who are incompatible with natural conception due to tubal or malefactors.

Conclusions:

Endometriosis is an enigmatic disease that impacts the quality of life of an adult and adolescent patient. The etiology remains unknown, though there are certain changes in the immune system as well as an association with abnormal outflow tracts. Endometriosis in infertile females is not uncommon & is increasingly being detected because of the greater use of diagnostic modalities like laparoscopy in the evaluation of infertility. Diagnostic delays are common and may lead to a decline in reproductive potential and fertility. But it is of limited value for diagnosing and determining the extent of endometriosis. Diagnosis is made by surgical visualization and treatment may involve hormonal manipulation and/or surgical ablation or resection. The surgical approach to endometriosis-associated infertility and pain has assumed a prominent role. Laparoscopy remains the gold standard for diagnosing and staging endometriosis.

The management of endometriosis-associated pain can be multifaceted, with surgical treatment as one of the options. With the exception of selected patients who are young and have relatively mild symptoms that respond to medical therapy, many patients during a diagnostic evaluation have a laparoscopy and subsequent treatment of endometriosis. The immunologic, genetic, and serum semi/non-invasive diagnostic biomarkers proposed to date for endometriosis diagnosis are not sufficiently sensitive and specific to justify their use as a screening test and thus improve outcomes, including less pain and better fertility. Medical treatments of endometriosis-associated infertility tend to ameliorate pain symptoms, but they are not effective in infertility treatment. These treatments should be utilized as an adjuvant to ART.

References

1. Cramer DW, Missmer SA. The epidemiology of endometriosis. Annals of the New York Academy of Sciences. 2002 Mar;955(1):11-22.

2. Rogers PA, D'Hooghe TM, Fazleabas A, Gargett CE, Giudice LC, Montgomery GW, Rombauts L, Salamonsen LA, Zondervan KT. Priorities for endometriosis research: recommendations from an international consensus workshop. Reproductive Sciences. 2009 Apr;16(4):335-46.

3. Zondervan KT, Becker CM, Missmer SA. Endometriosis. N Engl J Med 2020; 382:1244-56

4. World Bank. Population ages 15-64 (% of total population) | data, 2021. Available: https://data.worldbank.org/indicator/SP.POP.1564. TO.ZS

5. Eisenberg VH, Weil C, Chodick G, Shalev V. Epidemiology of endometriosis: a large population- based database study from a healthcare provider with 2 million members. BJOG: An International Journal of Obstetrics & Gynaecology. 2018 Jan;125(1):55-62.

6. Marci, R., Mallozzi, M., Di Benedetto, L., Schimberni, M., Mossa, S. & Soave, I. (2018). Radiations and female fertility. Reproductive Biology and Endocrinology. BioMed Central Ltd., 16: 1-12

7. Rajeswari M, Ramanidevi T, Kadalmani B. Cohort study of endometriosis in South Indian district. Int J Reprod Contracept Obstet Gynecol. 2016 Nov;5(11):3883-8.

8. Mishra VV, Gaddagi RA, Aggarwal R, Choudhary S, Sharma U, Patel U. Prevalence; characteristics and management of endometriosis amongst infertile women: a one-year retrospective study. Journal of clinical and diagnostic research: JCDR. 2015 Jun;9(6):QC01.

9. Leng JH, Lang JH, Dai Y, Li HJ, Li XY. Relationship between pain symptoms and clinico- pathological features of pelvic endometriosis. Zhonghua Fu Chan KeZaZhi. 2007;42(3):165-168.

10. Bulletti C, Coccia M E, Battistoni S, Borini A. Endometriosis and infertility. J Assist Reprod Genet. 2010;27(8):441-447

11. Buck Louis, G.M., Hediger, M.L., Peterson, C.M., Croughan, M., Sundaram, R. & Stanford, J. (2011). Incidence of endometriosis by study population and diagnostic method: The ENDO study. FertilSteril., 96(2): 360-5.

12. Zondervan KT, Cardon LR, Kennedy SH. What makes a good case-control study? Design issues for complex traits such as endometriosis. Hum Reprod2002;17:1415e23.

13. Evans MB and Decherney AH: Fertility and Endometriosis. Clin Obstet Gynecol. 60:497–502. 2017.

14. Grimstad FW, Decherney A. A review of the epigenetic contributions to endometriosis. Clinical obstetrics and gynecology. 2017 Sep 1;60(3):467-76.

15. Somigliana E, Vigano P, Benaglia L, Busnelli A, Berlanda N, Vercellini P. Management of endometriosis in the infertile patient. InSeminars in reproductive medicine 2017 Jan (Vol. 35, No. 01, pp. 031-037). Thieme Medical Publishers.

16. Janssen EB, Rijkers AC, Hoppenbrouwers K, Meuleman C, D'Hooghe TM. Prevalence of endometriosis diagnosed by laparoscopy in adolescents with dysmenorrhea or chronic pelvic pain: a systematic review. Hum Reprod Update 2013; 19:570e82.

17. Rowlands IJ, Abbott JA, Montgomery GW, Hockey R, Rogers P, Mishra GD. Prevalence and incidence of endometriosis in Australian women: a data linkage cohort study. BJOG: An International Journal of Obstetrics & Gynaecology. 2021 Mar;128(4):657-65.

18. American Society for Reproductive Medicine. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. FertilSteril. 1997; 67:817–21.

19. Zondervan, K.T., Becker, C.M., Koga, K., Missmer, S.A., Taylor R.N. &Viganò, P. (2018). Endometriosis. Vol. 4, Nature Reviews Disease Primers, p. 1-25.

20. Agarwal SK, Chapron C, Giudice LC, Laufer MR, Leyland N, Missmer SA, Singh SS, Taylor HS. Clinical diagnosis of endometriosis: a call to action. American journal of obstetrics and gynecology. 2019 Apr 1;220(4):354-e1.

21. Moradi, M., Parker, M., Sneddon, A., Lopez, V. & Ellwood, D. (2014). Impact of endometriosis on women's lives: A qualitative study. BMC Womens Health, 14(1).

22. Saceanu SM, Patrascu S, Patrascu A, Surlin V. Endometriosis: When and how we treat. Fertility- oriented Female Reproductive Surgery. 2017 Jan 18:61

23. Koninckx PR, Ussia A, Keckstein J, Wattiez A, Adamyan L. Epidemiology of subtle, typical, cystic, and deep endometriosis: a systematic review. Gynecological Surgery. 2016 Nov;13(4):457-67.

24. Boivin, J.; Bunting, L.; Collins, J.A.; Nygren, K.G. International estimates of infertility prevalence and treatment-seeking: Potential need and demand for infertility medical care. Hum. Reprod. 2007, 22, 1506–1512.

25. Riazi, H., Tehranian, N., Ziaei, S., Mohammadi, E., Hajizadeh, E. &Montazeri, A. (2015). Clinical diagnosis of pelvic endometriosis: A scoping review. BMC Womens Health. 15(1): 01.

26. Kvaskoff M, Mu F, Terry KL, Harris HR, Poole EM, Farland L, Missmer SA. Endometriosis: a high-risk population for major chronic diseases? Human reproduction update. 2015 Jul 1;21(4):500- 16.

27. Mcleod BS, Retzloff MG. Epidemiology of Endometriosis:: An Assessment of Risk Factors. Clinical obstetrics and gynecology. 2010 Jun 1;53(2):389-96.

28. Parazzini F, Esposito G, Tozzi L, Noli S, Bianchi S. Epidemiology of endometriosis and its comorbidities. European Journal of Obstetrics &Gynecology and Reproductive Biology. 2017 Feb 1;209:3-7

29. Parasar P, Ozcan P, Terry KL. Endometriosis: epidemiology, diagnosis and clinical management. Current Obstetrics and gynecology reports. 2017 Mar 1;6(1):34-41.

30. Kennedy S, Bergqvist A, Chapron C, Dhooghe T, Dunselman G, Greb R, Hummelshoj L, Prentice A, Saridogan E. ESHRE guideline for the diagnosis and treatment of endometriosis. Hum Reprod. 2005;20(10):2698–704.

31. Hsu AL, et al. Invasive and noninvasive methods for the diagnosis of endometriosis. Clin Obstet Gynecol. 2010;53(2):413–9.

32. De Ziegler D, Borghese B, Chapron C. Endometriosis and infertility: pathophysiology and management. The Lancet. 2010 Aug 28;376(9742):730-8.

33. Jacobson TZ, Duffy JM, Barlow DH, Farquhar C, Koninckx PR, Olive D. Laparoscopic surgery for subfertility associated with endometriosis. Cochrane Database of Systematic Reviews. 2010(1).

Table 3: Algorithm for a clinical diagnosis of endometriosis (21)

Algorithm for a clinical diagnosis of endometriosis	
Consistent with Endometriosis	Consider other Diagnosis in addition to Endometriosis
1) Evaluate the presence of symptoms	
• Persistent and /or worsening cyclic of constant pelvic pain • Dysmenorrhoea • Dyspanurea • Cyclic dysuria • Cyclic dyschezia • Cyclic catamenial symptoms located in other systems like lungs and skin	• Severe pain, amenorrhea, or cramping without mensuration in an adolescent could indicate reproductive tract anomaly. • Concomitant symptoms ✓ Severe non-cyclic constipation and diarrhoea ✓ Painful voiding of flank pain to suggest urinary tract stones ✓ Urinary symptoms to indicate interstitial cystitis/ painful bladder syndrome.
2) Review patient history	
• Infertility • Dysmenorrhoea in adolescents, current chronic pelvic pain. • Previous laparoscopy with a diagnosis • Dysmenorrhoea was unresponsive to NSAIDs. • Positive Family history	• Absence of menses or other obstructive conditions in adolescents. • History of pain directly associated with surgery.
3) Perform Physical Examination	
• Nodules in cul de sac • Retroverted uterus • Mass consistent with endometriosis • Obvious Endometrioma that is external	• Pelvic floor spasms • Severe allodynia along with pelvic floor/ vulva or elsewhere. • Masses not consistent with endometriosis.
4) Perform/ order imaging	
• Endometrioma on ultrasound • Presence of soft markers • Nodules/ Masses	• Adenomyosis and Fibroids

Table 4 Depicts: Risk factors for endometriosis (30)

Factors associated with increased risk	Factors associated with decreased risk
Earlier age at menarche	Parity
Shorter menstrual cycle length	Current oral contraceptive use
Taller height	Smoking
Alcohol use	Higher Body Mass Index
Caffeine intake	Regular exercise
	Fish and omega 3 fatty acids

Figure 1: Depicts Prevalence of Women Suffering from Endometriosis

Fig2: Depicts stages of Endometriosis A) Stage 1-Minimal B) Stage 2- Mild C) Stage 3 Moderate D) Stage 4-Severe

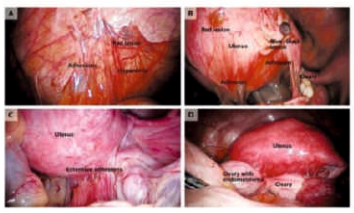


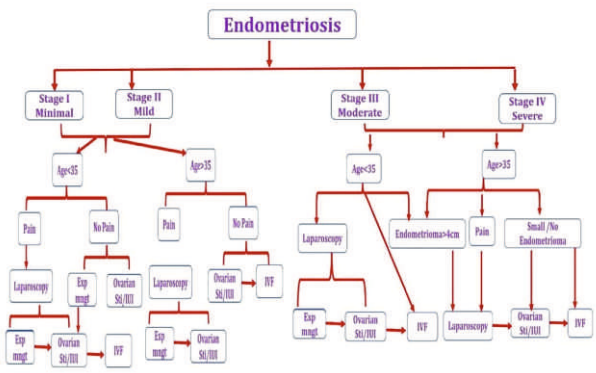
Table 1: rASRM Classification of Endometriosis(19). Stage I (Minimal)-1-5 cm, Stage II(Mild)- 6-15, Stage III (Moderate)-16-40, Stage IV (Severe)>40

	Endometriosis	Lesion <1 cm points	Lesion1 -3 cm points	Lesion>3 cm points
Peritoneum	Superficial	1	2	4
	Deep	2	4	6
Ovary	Right Superficial	1	2	4
	Deep	4	16	20
	Left Superficial	1	2	4
	Deep	4	16	20
	Posterior Cul -De-1997ac Obliteration	Partial		Complete
		4	40	
	Adhesions	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
Ovary	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
Tube	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16

Stage I	Hormonal Treatment and Surgery by laparoscopy
Stage II	IVF program but no hormonal treatment
Stage III	IVF followed by a hormonal treatment
Stage IV	No hormonal treatment, Laparoscopy for surgical treatment, or IVF

Table 2 depicts Treatment Proposals according to the Stages of Endometriosis

Fig 3 depicts Current Strategies For Endometriosis management for Different stages of Endometriosis



INVITED
ARTICLES

Artificial Intelligence In the Optimization and Personalization of fertility treatments

Dr Sweta Gupta
Medical Director, Crysta IVF
Reproductive medicine and IVF Consultant, Delhi/NCR
MBBS, MD (Obs & Gynae, Delhi)
MRCOG (London), DFSRH(UK), FRCOG (London)
MSc (Reproduction & Development, UK)
Fellowship in Reproductive medicine & ART (London, UK)
Editor IFS (22-24

What is Artificial intelligence (AI)?

AI is a "partnership between man and machine". It is a computer program that can learn to execute tasks involving human intelligence. It has the potential to enhance clinical decisions through algorithms, automated communication, and clinical imaging. It involves learning, self-adapting and predicting machine leading to transformation.

How is it used?

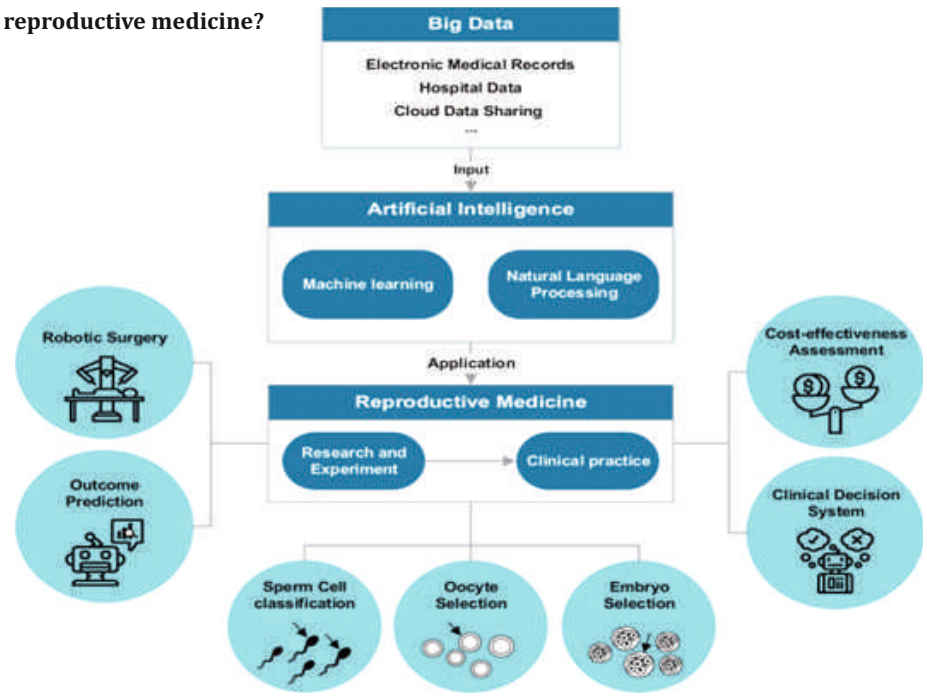
Reproductive experts can determine the best treatment for the individual infertility of patients by incorporating AI, machine learning (ML) and deep learning (DL).

Artificial intelligence (AI) is a science to build intelligent programs and machines that can creatively solve problems, which has always been considered a human prerogative.

Machine learning (ML) is a subset of AI that provide systems the ability to automatically learn and improve from experience without being explicitly programmed. In ML, there are different algorithms (neural networks) that help to solve problems.

Deep learning, or deep neural learning, is a subset of machine learning, which uses the neural networks to analyze different factors with a structure that is like the human neural system.

Where all AI can be used in reproductive medicine?



The role of AI in Reproductive Medicine. Big data include electronic medical records (EMRs) and other data. EMRs can capture data from various ways and the data is analyzed using AI such as machine learning and natural language processing (NLP). AI has been used in the many aspects of reproduction, from research and experiment to clinical practice. This schematic reviews the seven main applications of AI in reproductive medicine.

Wang R, Pan W, Jin L, et al. Artificial intelligence in reproductive medicine. Reproduction. 2019;158(4):R139-R154. doi:10.1530/REP-18-0523

Prediction of success rate: By constructing a functional IVF prediction model combined with AI, clinicians can tailor personalized treatment of subfertile couples and improve the pregnancy outcome of ART. Several papers have described models to predict IVF outcomes, where different AI methods have been used with the accuracies from 59 to 84.4%. Although the accuracy of predictions is gradually improving, there remain various problems and the model cannot be applied in clinical practice well. The age, antral follicle count, AMH, number of the developed embryos and endometrial thickness are the usual optimal predictive features.

Semen analysis and selection:

AI has been now used for semen analysis automatic evaluation, popularly called CASA (computerized assisted semen analysis). It has been also used for sperm morphology, DNA integrity as well as for sperm evaluating sperm morphology. AI can be applied for sperm selection. Due to the inherent lack of objectivity and the difficulty in the manual evaluation of the sperm morphology and the high degree of variation between laboratories, the automatic methods based on image analysis should be developed to gain more objective and precise results

Embryo selection:

It is an objective tool and can be divided into automatic annotation of embryo development (Cell stages and cell cycles), embryo grading and embryo selection for implantation. AI and machine learning are being used to analyze time-lapse imaging data with computer algorithms. AI analyses morphokinetic embryo development data as well as use of computer vision with image processing software to examine raw time-lapse images.

AI application showed in a study about 32% improvement in the prediction of successful implantation when compared to standard embryo morphological grading by highly skilled embryologists. AI algorithm that has outperformed human analysis, predicting human egg fertilization and blastocyst embryo development with 77% and 62% accuracy respectively.

Preimplantation Genetic Testing (PGT)

AI can be a useful prescreening tool that will allow us to identify and genetically test only those embryos that have a low likelihood of having genetic defects, lowering the overall cost of IVF for patients. AI is used to non-invasively analyze embryos and determine whether they are euploid or aneuploid. In fact, AI can be applied by deep learning through computer vision to embryo selection. AI was applied to PGT-A or interpretation and reporting of next-generation sequencing results (images) to eliminate operator subjectivity, ambiguous results and analyzing the impact of mosaicism.

Endometrial receptivity assessment and optimization

AI can be used for evaluation of defects in endometrium, used for visualization of uterine abnormalities. This evaluation can be used for prediction of implantation results. Machine learning–derived algorithm may assist clinicians in making an efficient and accurate initial judgment. Embryo receptivity assessment helps in transferring embryos at ideal time and thus improving success rates.

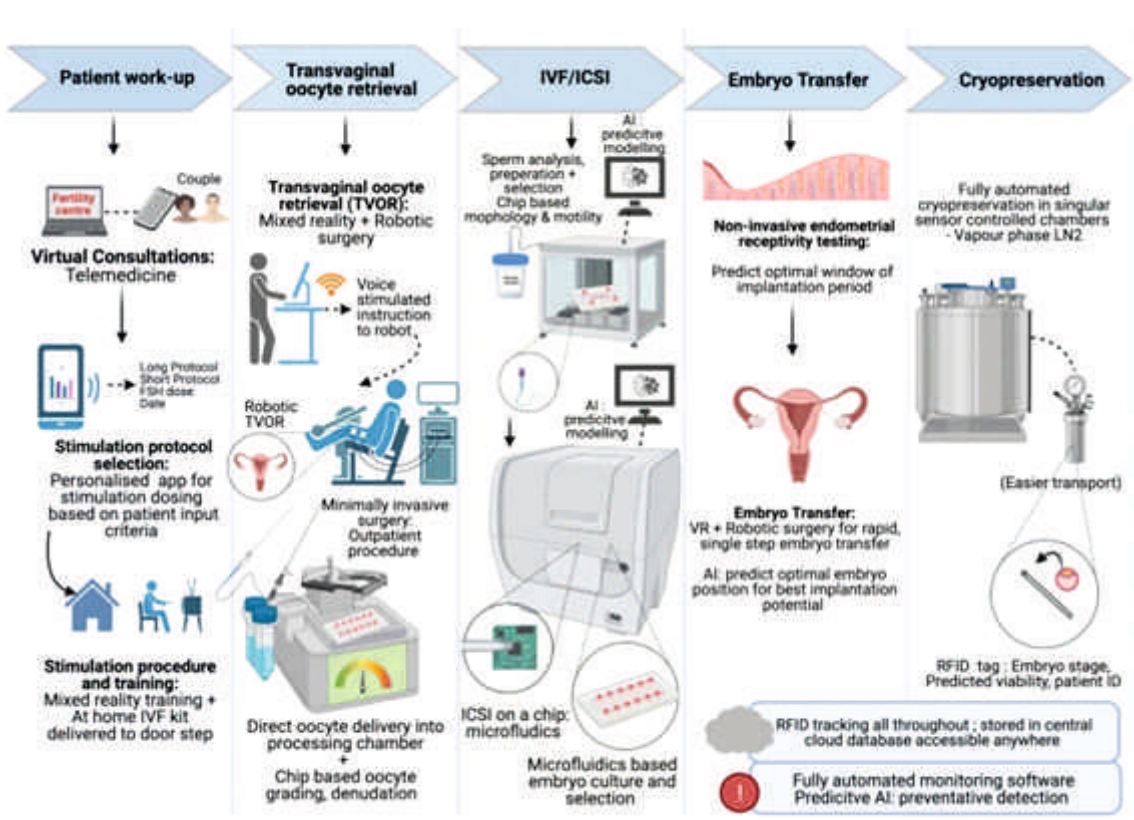
Miscarriage: Studies have reported up to 77% accuracy rate of pregnancy loss prediction, raising expectations that similar data may be used to prospectively select euploid embryos for transfer.

Quality control: AI can improve results by keeping quality control of a successful lab through automation, bringing objectivity to diagnostics and enhanced decision making rather than relying on limitations by human because of biases and subjectivity.

Advantages and Challenges:

An AI ART software can have many advantages like decrease interobserver variability, adjustment of drug doses in oocyte stimulation and thus reduce adverse effects such as hyperstimulation, decrease face-to-face medical contacts and thus increase medical and user productivity, better selection of sperm samples and evaluation of oocyte quality and embryo selection. Application of AI can be extended further by including patient characteristics like age, endocrine status, clinical diagnostics. AI lower mistakes in performing tasks regardless of the external environment, perform tedious repetitive tasks, organizing medical records and thus leads to digital transformation and automatization for the benefit of subfertile couples.

At the same time, it should be emphasized that computer can not completely replace human decision-making and substitute human compassion. There are however some other dilemmas like initial cost of deployment, the protection of personal data and corresponding legislation and the integration of human experience in clinical decision with ethical dilemmas of relying on machine to replace human decision-making.



Abdullah, K.A.L., Atazhanova, T., Chavez-Badiola, A. *et al.* Automation in ART: Paving the Way for the Future of Infertility Treatment. *Reprod. Sci.* (2022)

Conclusion:

AI application can help clinical decisions to be more accurate, prompt and objective. AI will not be able to replace reproductive medicine Consultants and embryologists but may improve clinical outcome. In future, the capabilities of AI techniques are likely to improve and may shorten time to pregnancy through improved IVF cycle efficiency (reduction of failed retrievals, transfers, miscarriages) and from replacement of a single, euploid embryo resulting in a healthy, live-birth. AI is an instrument to support clinical decision-making. Rapidly evolving state of innovations in artificial intelligence related automation in the patient treatment pathway, gamete/embryo selection, endometrial evaluation and cryopreservation of gametes/embryos has great future in increasing success rates, affordability and accessibility in infertility treatment.

INVITED
ARTICLES

Innovations in Ultrasound in ART

Dr Sarabjeet Singh
MBBS DGO PhD Fellow ART
Consultant Reproductive Medicine and Fertility Endoscopy

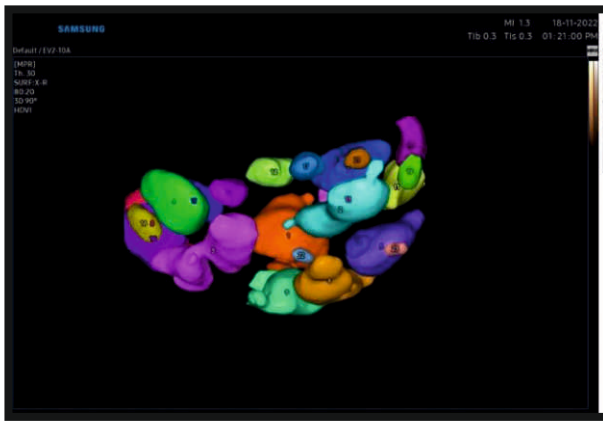
Introduction:

Assessment of the reproductive function of a woman is an important part of the fertility evaluation and pelvis ultrasound (esp. Transvaginal route) is typically used in this regard. The ultrasound evaluation of women for fertility work-up includes assessment of ovarian reserve, Development of follicle (s) in natural or stimulated cycles (Controlled Ovarian Hyperstimulation; COH in IVF), Rupture and formation of adequate corpus luteum and Development of endometrium in various phases of menstrual cycle in synchronous with developing follicle , Assessment of the uterine shape & size and Finding any Pathology in the pelvis which may have an impact on female fertility like Fibroids, Adenomyomas, Endometriomas, Hydrosalpinges and many more. . A 2D ultrasound is typically and most commonly used by most of the fertility professionals in this regard and 2D USG has proved itself to be sufficiently accurate and efficacious in the fertility treatment. The Recent advancements in the field of sonology with the advent of more advanced equipments having better resolution, incorporation and application of various innovative softwares, more frequent usage of 3D/4D USG in difficult case scenarios and better understanding of Coloured pulsed doppler has made fertility ultrasound more clinically rewarding and efficacious. This Chapter would focus on the newer innovations developed in the field of fertility sonology with an evidence-based evaluation of the technique available.

Assessment of the Follicle(s):

Conventionally, Follicular monitoring is done using a 2D Transvaginal ultrasound. The transverse and the longitudinal diameter of the follicle is measured and a mean is calculated to obtain mean diameter (1). This method has long been debated as it carries a lot of interobserver variability in measurements and also it lacks any standard protocol of measurement. It also becomes a time-consuming affair in COH-IVF where multiple follicles are to be measured individually. A study (2) proved that a follicle of 15 mm was measured 13- 18 mm by the same observer on two different occasions and 12-18 mm by multiple observers. Larger follicles had even a more tendency for measurement variabilities which potentially can impact the results of an IVF Cycle. A similar observation was made in few other studies which quoted 2D TVS measurement of follicle being less accurate. (3 & 4). Recently, application of 3D/4D USG has overcome these limitations of 2D USG. Whereas in 2D USG single focus is visualized, A 3D USG is collection of either manual or automated multiple 2D images which are interpreted in three dimensions to generate a 3D image. This 3D data can be used in real time mode to generate a 4D Image. Various innovative automated softwares like SonoAVC) Sonography-based Automated Volume) & VOCAL ((Virtual Organ Computer-aided Analysis)) are available which can be used in this regard (Picture 2). Various Advantages of using A 3D/4D over 2D are (5,6,7): (Image 1, 2)

Image 1 & 2: Automated 3D - 5D Follicle measurements



[Gynecology]

5D Follicle					
Lt. Ovary		D(V) [mm]		Count	
Follicles in Range		0 - 9		23	
No.	D(V) (mm)	V (cm^3)	Long (mm)	Short (mm)	Avg. (mm)
1	8.3	0.30	9.5	5.8	7.6
2	8.0	0.27	16.6	4.1	10.3
3	7.9	0.25	15.7	4.5	10.1
4	7.7	0.24	8.6	5.3	7.0
5	7.4	0.21	10.7	4.6	7.6
6	7.2	0.19	14.6	4.3	9.4
7	7.1	0.19	8.6	5.3	7.0
8	7.0	0.18	10.1	4.8	7.5
9	6.9	0.17	10.2	4.5	7.4

5D Follicle					
Lt. Ovary		D(V) [mm]		Count	
Follicles in Range		0 - 9		23	
No.	D(V) (mm)	V (cm^3)	Long (mm)	Short (mm)	Avg. (mm)
10	6.8	0.17	8.2	4.7	6.4
11	5.7	0.10	6.3	4.1	5.2
12	5.6	0.09	6.5	4.0	5.3
13	5.4	0.08	7.4	3.3	5.3
14	5.0	0.07	7.0	3.4	5.2
15	4.5	0.05	6.4	3.2	4.8
16	4.2	0.04	5.2	3.0	4.1
17	4.1	0.04	4.2	3.1	3.7
18	4.1	0.04	5.2	2.7	3.9
19	4.0	0.03	4.8	2.6	3.7
20	3.5	0.02	5.0	2.0	3.5
21	2.5	0.01	3.4	1.3	2.4
22	2.3	0.01	3.2	1.6	2.4

1. It standardises the measurement of follicle especially in COH-IVF thereby reducing the Intra / Interobserver variability

2. It is less time consuming as measurement of individual follicle is not needed. An automated mode in 3D/4D can obtain all measurements in few seconds.

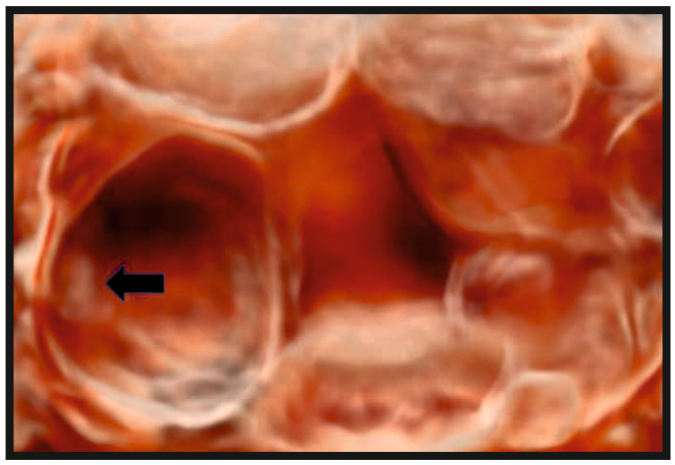
3. 3D USG provides a better Pictorial visualization of whole ovary with multiple follicles (in different colours) which are easily understood by the patient and helps in counselling.

4. One of the major advantages of 3D/4D USG is the calculation of the volume of the Region of Interest (ROI). A post-processing of the image with application of various modes (Inversion mode) can outline the boundaries of the organ better and helps in improved differentiation of the multiple structures around.

Pulsed Doppler use in Follicle monitoring:

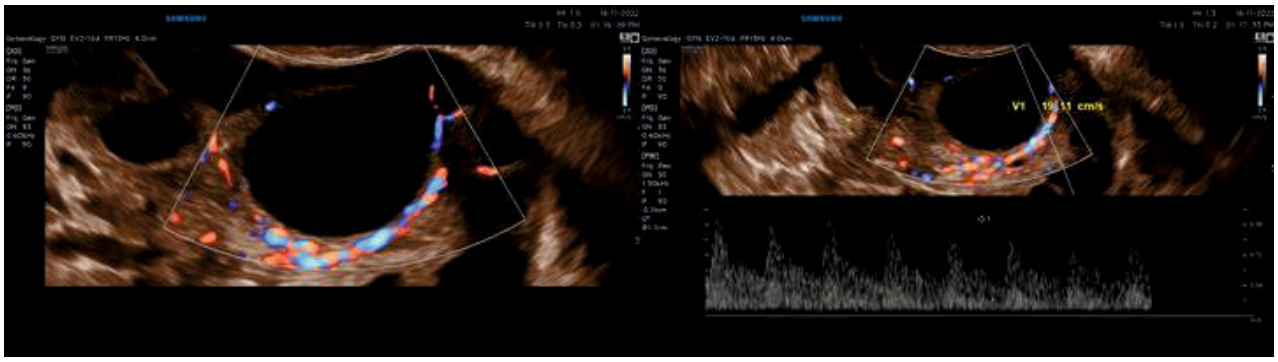
Conventionally, on 2D USG, Maturity of the Follicle is judged by Its size in synchrony with the Days of menstrual cycle along with the rising Estradiol values in the blood but relying only on the size of the follicle alone has been argued by many authorities as it may not reveal the maturity of the Oocyte complex. (8). The Physiological blood Flow changes happening in the growing follicle appears to be a better predictor of the maturity of the follicle and hence usage of 3D Power doppler has been advocated by many authorities for a better outcome of the stimulation. (9). Likewise, in Conventional 2D USG, it is difficult to locate and reproduce an Oocyte cumulus complex which can be visualized by newer 3D USG. In a study by Pohel et al, no oocyte complex was retrieved when a 3D USG failed to locate an OCC emphasising its relevance. (10) (Image 3)

Image 3: Cumulus Complex on 3D USG



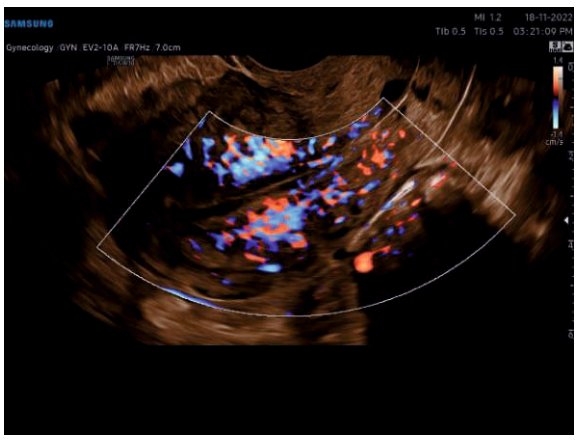
In physiological inactive ovaries as seen before menarche and after menopause, the ovarian stromal blood flow is negligible as ovaries are poorly vascularized. The RI/PI during these times is reported to be very high. As the female enters into reproductive age and menstrual cycle begins, Ovarian stromal blood flow starts increasing as depicted by gradual rise in PSV of stromal blood flow with lowering of RI &PI. The primordial and preantral follicles have virtually limited vascular flow. As the follicle grows, it starts developing its vascularity and can be assessed by calculating vascular flow over its circumference and PSV of Stromal blood flow. A mature follicle ready for the trigger can be defined when it has a vascularity occupying > ¾ th (>75%) of the periphery, PSV > 10-12 cm/s with RI of 0.40-0.48 of perifollicular vessels. An ideal follicular volume at this stage is considered 3-7.5 cc with Follicular vascularization index (VI) being 6-20 and FI > 35. (11,12). Other than deciding the timing of the trigger, Studies have depicted that colour doppler can be helpful in deciding dose of gonadotropins with higher doses needed in ovaries when stromal RI is high (> 0.56) on 2D Doppler and stromal flow index (FI) is less (< 11) in 3D Compared to lesser doses when ovarian RI < 0.50 in 2D Doppler and ovarian stromal blood flow is > 15 in 3D Doppler. (11) (Image 4,5)

Image 4 & 5: Perifollicular Doppler



Colour Doppler in Endometrium assessment: Endometrium development is a sign of growing follicle with a rising Estradiol values. On 2D USG, an Endometrial thickness of > 8mm with classical three-layered pattern morphology is generally considered sufficient for an embryo to implant. However, few studies depicted that vascularity rather than thickness and morphology of the endometrium is more important for an implantation to happen. As the follicle grows, the spiral arteries grow towards endometrium and penetrate into it. Applebaum (13) classified vascularity of the endometrium in four zones and defined a mature endometrium when vascularity reached zone 3-4 covering 5mm2 area with RI of endometrial arteries < 0.59. A low implantation with a higher chance of miscarriages was found in endometrium lacking these doppler parameters irrespective of the three-line morphological appearance and an appropriate thickness of > 8 mm. (Table 1) Similarly, calculating Endometrial volume on the day of HCG trigger and embryo transfer predicted chances of a successful implantation better than a conventional 2D ultrasound. In a study by Maged AM et al, a cut off of endometrial volume of 3.26 and 2.95 ml on the day of trigger and embryo transfer had 70 & 80% sensitivity, specificity 64.5 & 51.6%, a positive predictive value 38.9 & 34.8%, and negative predictive value 87.0 & 88.9%. (14) Since spiral arteries originate from uterine arteries, studies depicted that serial measurement of uterine artery doppler can be incorporated in the protocol to prognosticate and alter the IVF result. Steer et al,1992 Studied impact of uterine artery PI on the implantation of the embryo and categorized patients into three groups: low (1-1.99), medium (2-2.99) and high PI (>3) and found that no pregnancy resulted in high PI group. (15) (Image 6 & 7)

Image 6 &7: Endometrial Doppler a) Applebaum score: zone 4 vascularity b) Endometrial Volume



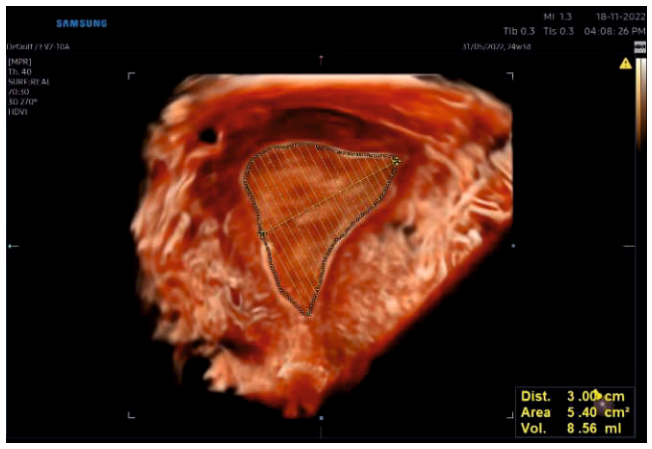


Table 1: Applebaum Scoring of Endometrial Vascularity	
Zone I	Blood vessels reaching till endo -Myometrial junction
Zone II	Blood vessels penetrating into endometrium till outer hyperechoic region
Zone III	Blood vessels penetrating into endometrium till hypoechoic zone
Zone IV	Blood vessels penetrating into endometrial cavity
Zone III & Zone IV vascularity is considered an "Ideal "and should cover a 5mm ^{2} area. The RI of endometrial vessels should be <0.50. The absence of above features could have a detrimental effect on Implantation of the embryo or can increase a chance of miscarriage.	

Ovarian Reserve Testing: Ultrasound evaluation of Ovary to assess the ovarian reserve is an important part of fertility assessment. On Conventional 2D ultrasound, it is done in initial follicular menstrual phase (Day2-3) by counting antral follicles (2-10 mm). Recent reports from the research exhibited that the size of AFC is more important rather than the count of AFCs and 2D USG has limitations in this regard. This fact was supported by a study from Saumet et al, which proved that AFC measurement using 3D Sonogram correlated equally with AMH and 2D USG proved inferior in this regard. (16,17) Similarly, Measuring Ovarian volume in early follicular phase before development of a dominant follicle with 3D has been advocated by few researchers. It helps in predicting the ovarian response during IVF stimulation with ovaries having volume < 3 ml either had more cancellation of the cycles or yielded poor number of oocytes. (17)

Congenital uterine Anomalies:

CUA are more frequently seen in infertile patients and patients with a history of recurrent miscarriage. The diagnosis of CUA in these cases is of paramount importance as it may prognosticate the outcome of the fertility treatment and obstetrical consequences like Preterm birth and Miscarriages. (18) A diagnostic laparoscopy with hysteroscopy was considered gold standard in evaluation a case of CUA but is associated with limitations of being an invasive procedure and carries a risk of surgical and aesthetic complications. 2D ultrasound is insufficient to correctly make a diagnosis in this regard as it focuses on a single plane at a time. Hysterosalpingography and recently sonohyterography or HyCoSy are often used as a first tool but HSG can only demarcate the internal lining (contour) of the uterus and is not accurate in subtle anomalies as well as differentiating anomalies like subspetate from bicornuate uterus. A 3D-4D USG can be more yielding in diagnosing and differentiating various uterine animalities with sensitivity and specificity equal to MRI. When compared to HSG and 2DUS, 3DUS demonstrates high sensitivity and specificity for the identification of a normal uterus (98 and 100 %), arcuate uterus (100 and 100 %), or major uterine anomaly (100 and 100 %). In comparison, 2DUS has lower sensitivity and specificity for the diagnosis of a normal uterus (88 and 94 %) or arcuate uterus (67 and 94 %), but is similarly accurate with major uterine anomalies (100 and 95 %). Hence, 2DUS may be best utilized as a screening test for uterine anomalies, with 3DUS as the definitive diagnostic test. (19) Also, 3DUS assessment of the uterine fundus correlated 91.6 % with laparoscopic findings, and evaluation of the uterine cavity correlated 100 % with hysterosalpingography. (19)

Table 2: 3D ultrasound criteria for classification of congenital uterine anomalies

Uterine morphology	Fundal contour	External contour
Normal	Straight or convex	Uniformly convex or with indentation <10 mm
Arcuate	Concave fundal indentation with central point of indentation at obtuse angle (>90°)	Uniformly convex or with indentation <10 mm
Partial septate	Presence of septum (does not extend to cervix) with central point of septum at an acute angle (<90 %)	Uniformly convex or with indentation <10 mm
Complete septate	Presence of septum that completely divides cavity from fundus to cervix	Uniformly convex or with indentation <10 mm
Bicornuate	Two well-formed uterine cornua	Fundal indentation >10 mm dividing the two cornua
Unicornuate uterus	Single well-formed uterine cavity with a single interstitial portion of fallopian tube and concave fundal contour	Fundal indentation >10 mm dividing the two cornua if a rudimentary horn is present
Normal	Straight or convex	Uniformly convex or with indentation <10 mm

A double endometrial echo complex as seen on a transverse plane with 2D ultrasound is indicative of a uterine anomaly but this is observed with arcuate, septate and bicornuate uteri . A unicornuate on 2D USG will not have double endometrial echo complex and is hard to visualize on it.

Conclusion:

The Current developments in the field of sonology with the advent of more advanced equipments with better resolution and integration with various innovative softwares has made the evaluation and procedures related to the field of fertility more rewarding and successful. In particular, 3D/4D USG in difficult case scenarios and better understanding of Coloured pulsed doppler has made a great contribution in overall success of a fertility treatment.

References:

1. Re C, Mignini Renzini M, Rodriguez A, Dal Canto M, Buccheri M, Sacchi S, Bartolucci S, Fadini R, La Marca A. From a circle to a sphere: the ultrasound imaging of ovarian follicle with 2D and 3D technology. Gynecol Endocrinol. 2019 Mar;35(3):184-189. doi: 10.1080/09513590.2018.1522297. Epub 2018 Nov 3. PMID: 30394144.

2. R.G. Forman, J. Robinson, P. Yudkin, D. Egan, K. Reynolds, D.H. Barlow What is the true follicular diameter: an assessment of the reproducibility of transvaginal ultrasound monitoring in stimulated cycles Fertil Steril., 56 (1991), pp. 989-992

3. Sauerbrun, May-Tal MD; Ghidei, Luwam MD; Huber, Warren J. MD; Wu, Xiaotian; Alvero, Ruben MD; Wang, Shunping PhD. 3-D Ultrasound is Accurate for Follicular Monitoring But Does Not Reduce Time to Perform [28S]. Obstetrics & Gynecology: May 2019 - Volume 133 - Issue - p 209S-210 doi: 10.1097/01.AOG.0000559479.77504.aa

4. N. Raine-Fenning, K. Jayaprakasan, J. Clewes Automated follicle tracking facilitates standardization and may improve work flow Ultrasound in obstetrics & gynecology: the official journal of the International Society of Ultrasound Obstet Gynecoly., 30 (2007), pp. 1015-1018 doi: 10.1002/uog.5222

5. Rodriguez A, Guillén JJ, López MJ, Vassena R, Coll O, Vernaeve V. Learning curves in 3-dimensional sonographic follicle monitoring during controlled ovarian stimulation. J Ultrasound Med. 2014 Apr;33(4):649-55. doi: 10.7863/ultra.33.4.649. PMID: 24658944.

6. Murtinger M, Aburumieh A, Rubner P, Eichel V, Zech MH, Zech NH. Improved monitoring of ovarian stimulation using 3D transvaginal ultrasound plus automated volume count. Reprod Biomed Online. 2009 Nov;19(5):695-9. doi: 10.1016/j.rbmo.2009.09.008. PMID: 20021717.

7. Raine-Fenning N, Jayaprakasan K, Deb S, Clewes J, Joergner I, Dehghani Bonaki S, Johnson I. Automated follicle tracking improves measurement reliability in patients undergoing ovarian stimulation. Reprod Biomed Online. 2009 May;18(5):658-63. doi: 10.1016/s1472-6483(10)60010-7. PMID: 19549444.

8. Agrawal S, Panchal S, Nagori C. Relationship between Follicular Volume, Oocyte Competence, and Blastocyst Development in ART. Donald School J Ultrasound Obstet Gynecol 2020; 14 (2):136-143.

9. Panchal S, Nagori CB. Pre-hCG 3D and 3D power Doppler assessment of the follicle for improving pregnancy rates in intrauterine insemination cycles. J Hum Reprod Sci. 2009 Jul;2(2):62-7. doi: 10.4103/0974-1208.57224. PMID: 19881150; PMCID: PMC2800929.

10. Poehl M, Hohlagschwandtner M, Doerner V, Dillinger B, Feichtinger W. Cumulus assessment by three-dimensional ultrasound for in vitro fertilization. Ultrasound Obstet Gynecol. 2000 Sep;16(3):251-3. doi: 10.1046/j.1469-0705.2000.00270.x. PMID: 11169291.

11. Sharma N, Saravanan M, Saravanan Mbbs L, Narayanan S. The role of color Doppler in assisted reproduction: A narrative review. Int J Reprod Biomed. 2019 Dec 26;17(11):779-788. doi: 10.18502/ijrm.v17i10.5484. PMID: 31911960; PMCID: PMC6906874.

12. Costello MF, Shrestha SM, Sjoblom P, McNally G, Bennett MJ, Steigrad SJ, Hughes GJ. Power Doppler ultrasound assessment of ovarian perifollicular blood flow in women with polycystic ovaries and normal ovaries during in vitro fertilization treatment. Fertil Steril. 2005 Apr;83(4):945-54. doi: 10.1016/j.fertnstert.2004.09.025. PMID: 15820805.

13. Applebaum M. The uterine biophysical profile. Ultrasound Obstet Gynecol. 1995;5(1):67–68. doi: 10.1046/j.1469-0705.1995.05010067.x.

14. Maged AM, Kamel AM, Abu-Hamila F, Elkomy RO, Ohida OA, Hassan SM, Fahmy RM, Ramadan W. The measurement of endometrial volume and sub-endometrial vascularity to replace the traditional endometrial thickness as predictors of in-vitro fertilization success. Gynecol Endocrinol. 2019 Nov;35(11):949-954. doi: 10.1080/09513590.2019.1604660. Epub 2019 Apr 21. PMID: 31007123.

15. Steer, C V et al. "The use of transvaginal color flow imaging after in vitro fertilization to identify optimum uterine conditions before embryo transfer." Fertility and sterility 57 2 (1992): 372-6 .

16. Peres Fagundes PA, Chapon R, Olsen PR, Schuster AK, Mattia MMC, Cunha-Filho JS. Evaluation of three-dimensional SonoAVC ultrasound for antral follicle count in infertile women: its agreement with conventional two-dimensional ultrasound and serum levels of anti-Müllerian hormone. Reprod Biol Endocrinol. 2017 Dec 16;15(1):96. doi: 10.1186/s12958-017-0314-x. PMID: 29246176; PMCID: PMC5732451.

17. Saumet J, Dzineku F, del P, Velez M, Jamal W, Lehmann P, et al. Evaluation of the ovarian reserve: is there still a place for ultrasound? Fertil Steril (2012) 98:S38–9 10.1016/j.fertnstert.2012.07.144

18. Kim MA, Kim HS, Kim YH. Reproductive, Obstetric and Neonatal Outcomes in Women with Congenital Uterine Anomalies: A Systematic Review and Meta-Analysis. J Clin Med. 2021;10(21):4797. Published 2021 Oct 20. doi:10.3390/jcm10214797

19. Rackow, B.W. (2014). Congenital Uterine Anomalies. In: Stadtmauer, L., Tur-Kaspa, I. (eds) Ultrasound Imaging in Reproductive Medicine. Springer, New York, NY. https://doi.org/10.1007/978-1-4614-9182-8_9

INVITED ARTICLES

NEWER CONCEPTS ON SEXOLOGY

Dr Rajapriya Ayyappan
MD DNB FRCOG (UK) FRM & Sexology
Srinivas Priya Hospital , Chennai

Sexology is the scientific study of human sexuality, including human sexual interests, behaviours, and functions, it is shaped by our upbringing ,attitudes ,physical appearance,values ,personality and our social outlook. Covid pandemic has brought to light the changing aspects of sexuality and sexual trends .Many were forced to use gadgets and social media to connect to their loved ones, we even had a hindi movie to depict the struggle to keep alive **long distance relationship**, probably the couples of today are comfortable to be sexually active, very rarely physically but be more connected non physically on a regular basis using zoom etc- **zoom sex**. It is said there was a boom of sex toys sale in peri covid period ,proving that single person also can be sexually satisfied using the wide range of amazon products ,eg vibrators to arouse their delicate private parts like clitoral and penile sensations. Another interesting development is the focus on overall health and body ,oral ,hand and **sexual hygiene** which actually enhances the odour free ,enhanced sexual experience of the couple. Participating in regular exercise or sports activity as a couple to **boost body building immunity** is a new found hobby, thanks to corona virus !! **Sexual mindfulness** ,thinking beyond Orgasm as the only sexual climax but to appreciate the very small activities of physical closeness like kissing ,hugging, touching, caressing can equally contribute to holistic sexual health between couples.

Sex is more than procreation, creation, but can also be healing, and transformational. Bliss states linger longer once the orgasm is over. After the covid crisis, most people reflect to be more attentive about connecting with their partner at a deeper level.Sexual behavior is all about knowing each other better and trying to connect at the mind ,body and soul level!Communication and understanding the needs of each other, has improved sexual compatibility.Many partners all around the world finally found a lot of time for each other,to care,to cope ,to love and to have sex regularly and to be able to enjoy it! While others realised that they are a mismatched couple and this needs to stop and part ways forever as they are not meant to be together! Newer concepts and discoveries of sexuality are contributed by sociologists ,psychologists and sexologists.

There has always been an assigned social definition for gender roles as FEMININE AND MASCULINE but today we are bridging up ,with changing social behaviour and started accepting GENDER EQUALITY .It is upto the individual to take up a chosen identity that suits best, as his or her GENDER IDENTITY! It is important to help our ADOLESCENTS discover their sexuality and build up positive sexual health through scientific and professional SEXUAL HEALTH AWARENESS AT SCHOOLS AND COLLEGES rather than inputs by uncontrollable social media and peers! SEXUAL RIGHTS to make free and responsible reproductive choices must be available to all. The newer concepts must be grasped and improved upon by the different diverse generations and successfully intergrate it into the Traditional core concepts of healthy sexual living !

Let us know the 12 Indian laws relating to sex ,keeping pace with a changing society ,soon Same Sex marriage may get legally recognised and Marital Rape can get criminalised!

1. You can have sex with your partner without being married to them,consensual sex is Allowed between two homosexual or heterosexual patners ,in private

2. However,same sex marriage is not legally accepted

3. Live in relationship is not illegal between unwed partners

4. A child born out of a live-in relationship is legitimate. If the couple lived together for a significant time, the law would presume them married.

5. Two consenting adults are allowed to check in a hotel in India with valid ID proofs. However ,most hotels won't do so ,as we are still a conservative society!

6. Every woman whether married or unmarried is allowed to terminate unwanted pregnancy up to 20 weeks of gestation period. In cases of reserved categories of women who are minors or rape & incest survivors, the termination limit has been extended up to 24 weeks.

7. Hanging out with partners in public places is legally allowed.As per Section 294 of the Indian Penal Code, the act of obscenity causing "annoyance of others" can be punished with a fine and imprisonment of up to 3 months. However, what's considered obscene still remains highly subjective since the law is not very clear about it. The word often gets brutally exploited because of conservatism in our society.

8. Currently ,Marital rape is not a crime in India.

9. The Protection of Women from Domestic Violence Act, 2005 ,acknowledges the right of a woman who was in a live in or marital relationship with a person , to seek protection against domestic violence.

10. India is one of the leading hubs of the commercial sex industry. Apparently, in our country, private prostitution is not illegal per se. However, associated activities such as child prostitution, human trafficking, running a brothel, prostitution in a hotel, and pimping are illegal. Supreme court of india recognises legally rights of a PRIVATE SEXUAL WORKER .

11. Unmarried couples can rent and even buy a house together.

12. The Transgender Persons (Protection of Rights) Act, 2019 recognizes the right to self-perceived gender identity, thus allowing transgender people to register themselves under a third gender (transgender). However, identification as male or female can only be issued once proof of gender confirmation surgery

Lesbian, gay, bisexual and transgender and queers(LGBTQ) rights in India have been evolving rapidly in recent years. Homophobia is prevalent in India, Public discussion of homosexuality in India has been inhibited by the fact that sexuality in any form is rarely discussed openly. In recent years, however, attitudes towards homosexuality have shifted slightly. In particular, there have been more depictions and discussions of homosexuality in the Indian media and cinema which has helped acceptance. India is among countries with a social element of a third gender but holistic support from family,society and police is the need of the hour . Mental, physical, emotional and economic violence against the LGBT community in India continues to be a problem. RIGHT TO CHANGE GENDER ,government provides Ayushman bharat health insurance cover for gender reassignment since 2022. The ancient Indian text Kamasutra written by Vātsyāyana dedicates a complete chapter on erotic homosexual behaviour. Historical literary evidence indicates that homosexuality has been prevalent across the Indian subcontinent throughout history.

Sexual behaviour is progressive and ADAPTIVE if we understand and respect the RIGHTS of others .MALADAPTIVE response leads to DYSFUNCYION in sexual performance and can lead to PERVERSION causing harm,force towards their partners.MODERN SOCIETY can be as revolutionary and welcoming to all types of sexuality as variations of accepted normal !But the danger is,it can encourage sexual abuse ,domestic violence,commercial exploitation of sex in the minds of some ANTI SOCIAL PERSONALITIES ! Too much of freedom can be a decision challenge for TODAY'S INDIANS, as sexuality is in a liberalized phase .Until now most of us, have had thoughts and conversations on sex only with oneself in privacy ,it has been a taboo to openly express oneself publicly ,until recently! Sexuality is sum total of our sexual feeling and the behaviour.Currently ,INDIAN sexuality stands more liberalized than before but still it is on a legal and moral policing leash!

INVITED
ARTICLES

Reproductive Genetics and Infertility

Dr Umesh N Jindal
Dr Sangeeta Khatter
Jindal IVF and Sant Memorial Nursing Home, Chandigarh

The physiology of reproduction involves several paracrine, autocrine, and endocrine processes regulated by different genetic mechanisms (Rodrigues VO,2020). Infertility is a complex disorder of the reproductive system, defined as the inability to get pregnant after more than 12 months of regular and unprotected sexual intercourse and affects more than 75 million couples of reproductive age in the world (Tomaiuolo,2021).

The importance of genetics in reproductive field started with the implementation of chromosome testing in the 1960s, a long time before the advent of in vitro fertilization.Traditionally it is known that genetic disorders are untreatable which leads to reluctance among Clinicians to invest on genetic diseases. However, the old concept is changing now. Genetics the fastest developing science is proving its role in management of infertility also similar to every discipline of medicine.

The major contribution of genetics is to predict and prevent a disorder thus decreasing its burden right from the planning of of a pregnancy(Ashutosh H,2016).It is observed that each of us carries at least 50-100 heterozygous variations. About 50% of first trimester abortions are associated with chromosomal defects. Approximately 0.2% babies are born with balanced structural chromosome rearrangement with implications on reproduction later in life.The proportion of chromosomal anomalies detected in stillbirths and neonatal deaths is around 5.6%- 11.5%. Three to four percent of all births are associated with a major congenital malformation or genetic disorders and this rate doubles by 8 years of age after inclusion of late appearing or diagnosed genetic disorders. Genetics contributes to infertility in approximately 15% cases as of now but this percentage is going to increase soon as many newer genetic, genomic and epigenetic factors are being recognized. The above-mentioned statistics indicates that no scientific stream has more genetic impact on the practice than reproductive process(Halder A,2015).

To fulfil the objectives of dealing with the genetic issues related to reproduction, a new branch known as Reproductive Genetics has emerged. This is a branch of science that deals with the genetic contribution of reproductive process, both natural and assisted.This stream is becoming an integral part of today's reproductive practice due to increase in the burden of reproductive disorders. The ideal time to apply reproductive genetics is from the time of pre-conception or peri-conception period because newer genomic technologies can be incorporated for diagnosis, prevention as well as prediction in this period only (Halder A, 2015). The infertility is the major area covered in reproductive genetics.(Garcia-Herrero,2020). Practically every genetic disorder might directly or indirectly interfere with fertility. Genetic causes must be ruled out before attempting any therapeutic procedure to reverse infertility, because infertility might be a selection mechanism devised by nature to prevent malformations (Coco R,2018).

Applications of reproductive genetics

Various applications of reproductive genetics in infertility and ART are discussed below:

Male Infertility

Genetic factors are identified in all the aetiologies of male fertility (pre-testicular, testicular and post-testicular). More than 200 genetic conditions related to male infertility are reported, ranging from the most common clinical presentations of infertility to the rarest complex syndromes which are not isolated to reproductive problems(CariatiF,2019). Currently, approximately 30% of male factor infertility is associated with known genetic causes. These causes include chromosomal abnormalities (Klinefelter syndrome), Yq microdeletion, Copy number variations (CNVs), monogenic, multi factorial, epigenomic, mitochondrial abnormalities etc. Infertile males with oligo/astheno/teratozoospermia (with normal blood Karyotype) have ten-fold increase of chromosomal abnormalities in their sperms, including diploidy, disomy and nullisomy. Based on prevalence data, routine karyotyping of infertile men within explained spermatogenic failure is widely recommended before ART. Monogenic disorders associated with male infertility are cystic fibrosis transmembrane receptor (CFTR) gene mutations in men with bilateral absence of the vas deferens,Kalman syndrome, Laurence Moon Biedl syndrome, Prader Willi syndrome, Noonan syndrome, androgen receptor mutations or CAG triplet expansion, 5 α-reductase deficiency, FSH-receptor mutation, LH receptor defects, mitochondrial gene defects, etc.(HalderA,2015).Genetic causes carry a significant prognostic value even if identified in minority of men with infertility. For example, in men with Yq microdeletions, testing of AZF has a prognostic impact for sperm extraction, since no sperm can be retrieved in AZFa and AZFb, while there is a fair chance in AZFc(Halder A,2015).The identification of additional genetic causes of male infertility would be helpful for patient counseling regarding diagnosis, potential treatments, outcomes of sperm retrieval, and ART.

Female Infertility

Female infertility has complex multifactorial origin as depicted by the clinical and genetic heterogeneity of the cohorts under study, hundreds of genes must interplay in a precise manner during sex determination, gametogenesis, complex hormone actions or interactions and embryo implantation. About 10% of infertility is due to premature ovarian insufficiency (POI). POI is highly clinically heterogeneous and is associated either with ovarian dysgenesis reflected by primary amenorrhoea or with secondary amenorrhoea. Most POI cases are 'idiopathic'. Chromosomal aberrations remain a major known cause of premature ovarian insufficiency (POI). Two loci on Xq22-q26 and Xq27-q28 appear to be critical (DIAPH2 gene in proximal Xq22, XPNPEP2 gene in Xq25, DACH2 gene in Xq21.3 and POF1B gene in Xq21.3) for the POI (AshutoshH, 2016). Among the monogenic causes, the CGG nucleotides expansions in the 'premutation range' in the FMR1 gene remain a well-established cause of isolated POI, more frequent in families with Fragile X syndrome than in sporadic cases of POI.Other monogenic syndromic associations with POI areBlepharophimosis–ptosis-epicanthus inversus syndrome(FOXL2 mutations) galactosemia (GALT mutations), congenital adrenal hyperplasia(CYP21A2 mutations), Progressive external ophthalmoplegia, a mitochondrial disease(POLG mutations),Perrault syndrome(CLPP, HARS2, HSD17B4, LARS2 and TWNK mutations), congenital disorders of glycosylation(PMM2and CLPP mutations), leukoencephaly with vanishing white matter syndrome(EIF2B2 mutations). Recently, dominant negative disease-associated variants in the TUBB8 gene, causing defects in spindle assembly and leading to oocyte maturation arrest, have been described in several families. FSH receptor (FSHR) variation (the p. Asn680Ser 'polymorphism') has clinical utility due to its defined predictive value and this variation is also linked to some cases of POI (Harper JC,2018).Although the existence of the genuine empty follicle syndrome is still in controversial phase, disease-associated variants in the LH/CG receptor gene (LHCGR) have been reported in this disorder.The pharmacogenomics research focusing on the identification of genetic variation related to the individual response to controlled ovarian hyperstimulation (COH) is going on.

Genetic mechanisms behind other aetiologies, such as hypothalamic–pituitary–gonadal deficiencies are also underway. Genome wide association studies (GWAS) have improved our genetic understanding of the common multifactorial disorders such as polycystic ovary syndrome (PCOS) and endometriosis, each affecting around 10% of women with female infertility. In PCOS, better patient stratification and functional genomics could provide novel research avenues while in endometriosis, abnormal epigenetic mechanisms in stromal cells are being proposed to play pathogenic role. (HarperJC, 2018).

Preconception carrier screening

ARTs implemented and enforced by personalized genomic medicine have provided the solutions to millions of infertile patients to have babies. Nonetheless, having a baby is not the only challenge to overcome in the reproductive journey, the most important is to obtain a healthy baby free of any preventable genetic condition which is a global health priority. This becomes especially important in some ethnic communities or populations where the incidence and levels of consanguinity are higher. The impact of genetic disorders during childhood is high, representing 20-30% of all infant deaths and 11.1% of paediatric hospital admissions. With these data, obtaining a precise genetic diagnosis is one of the main aspects of a preventive medicine approach in developed countries. The need of screening has led to advent of Genome-wide technologies along the different stages of the reproductive health lifecycle from preconception carrier screening and pre-implantation genetic testing, to prenatal and postnatal testing. (Darshan P. Patel,2020). Carrier screening is used to identify individuals or couples that are at risk to have a child with an autosomal recessive or X-linked genetic disorder. The identification of couples at risk of transmitting a specific inherited disorder to their offspringoffers the possibility of making informed reproductive choices to future parents (Cariati F,2019). The American College of Obstetricians and Gynaecologists has issued standard recommendations for ethnic and general population genetic screening in couples based on reproductive age. Testing is available for more than 2000 genetic disorders, including common diseases, such as thalassemia, sickle-cell anaemia, cystic fibrosis, and spinal muscular atrophy, Congenital adrenal hyperplasia or more complex conditions, such as mental retardation and congenital heart disease(Gregg, A.R,2021).

Prenatal screening and diagnosis

Prenatal testing and diagnosis(PND) has been the traditional strategy for reducing the burden of genetic disorders and congenital disabilities that cause significant postnatal functional impairment. Universal prenatal screening is advisable for common genetic disorders and congenital anomalies such as Down syndrome, beta-thalassaemia, and neural tube defects (PhadkeSR,2017). Invasive PND is usually performed on DNA extracted from fetal cells obtained by chorionic villus sampling (CVS) (between the 11th and 13th weeks of gestation) or from amniocytes (from the 15th to the 20th week). The molecular diagnosis for monogenic diseases can also be carried out depending upon the indications and turnaround time (Allyse M,2015). An increasing amount of interest has been shown regarding the non-invasive prenatal screening (NIPS) of cell-free fetal DNA (cfDNA) for the screening of chromosomes 21, 18, 13, X and Y and has been clinically adopted as well.

Preimplantation genetic testing (PGT)

PGT has the same diagnostic motivation as the traditional PND, with the advantage of advancing the timing of diagnosis at the embryo stage. These two diagnostic procedures share the same purpose but differ in diagnostic time, type of sampling, and laboratory procedures. PGT has the advantage of reducing the time to pregnancy and avoiding the cost, physical burden of repeated abortions and psychological trauma associated with PND. In addition to the more traditional laboratory investigations, it is now undisputed that molecular biology methods for PGT support the efficacy of ART techniques, contributing significantly to their success (reductions in time, effort, and cost (Cariati, F,2019).

Only disease-free embryos are transferred to the mother, avoiding recourse to therapeutic abortion. Even for couples who can conceive naturally, PGT requires the application of IVF techniques, including (a) the collection of gametes from both partners; (b) the fertilization of the oocyte by intracytoplasmic sperm injection (ICSI); (c) the embryo biopsy, which allows one or more cells from the blastomere or trophectoderm to be taken 3 or 5 days, respectively, postfertilization; (d) molecular analysis and (e) the embryo transfer.

Future applications

Mitochondrial replacement in human oocytes and to cross-generational epigenetic inheritance or germline genome editing (GGE) technologies are gradually creating paradigm shifts in the field of ART(HarperJC,2018).

References:

1. *Rodrigues VO, Polisseni F, Pannain GD, Carvalho MAG. Genetics in human reproduction. JBRA Assist Reprod. 2020 Oct 6;24(4):480-491. doi: 10.5935/1518-0557.20200007. PMID: 32293822; PMCID: PMC7558894.*

2. *Tomaiuolo, R. Genetics and Genomics of Reproductive Medicine. Genes 2021, 12, 1612. https://doi.org/ 10.3390/genes12101612*

3. *Ashutosh Halder (2016) Reproductive Genetics. J Clin Diagn Res 4: 106. doi:10.4172/2376-0311.1000e106.*

4. *Halder A(2015)Reproductive Genetic Counselling in Genomic Era. EC Gynaecology 2 : 132-148.*

5. *Garcia-Herrero S, Simon B, Garcia-Planells J. The Reproductive Journey in the Genomic Era: From Preconception to Childhood. Genes (Basel). 2020 Dec 19;11(12):1521. doi: 10.3390/genes11121521. PMID: 33352697; PMCID: PMC7767043.*

6. *Coco R. Genetic counseling prior to Assisted Reproductive Technology procedures in the era of cytogenomics. JBRA Assist Reprod. 2018 Nov 1;22(4):375-380. doi: 10.5935/1518-0557.20180050. PMID: 30106543; PMCID: PMC6210621.*

7. *Cariati, F., D'Argenio, V. &Tomaiuolo, R. The evolving role of genetic tests in reproductive medicine. J Transl Med 17, 267 (2019). https://doi.org/10.1186/s12967-019-2019-8*

8. *Harper JC, Aittomäki K, Borry P, Cornel MC, de Wert G, Dondorp W, Geraedts J, Gianaroli L, Ketterson K, Liebaers I, Lundin K, Mertes H, Morris M, Pennings G, Sermon K, Spits C, Soini S, van Montfoort APA, Veiga A, Vermeesch JR, Viville S, Macek M Jr; on behalf of the European Society of Human Reproduction and Embryology and European Society of Human Genetics. Recent developments in genetics and medically assisted reproduction: from research to clinical applications. Eur J Hum Genet. 2018 Jan;26(1):12-33. doi: 10.1038/s41431-017-0016-z. Epub 2017 Dec 4. PMID: 29199274; PMCID: PMC5839000.*

9. *Darshan P. Patel, Tim G. Jenkins, Kenneth I. Aston, Jingtao Guo, Alexander W. Pastuszak, Heidi A. Hanson, James M. Hotaling,Harnessing the full potential of reproductive genetics and epigenetics for male infertility in the era of "big data",Fertility and Sterility,Volume 113, Issue 3,2020,Pages 478-488,ISSN 0015-0282,https://doi.org/10.1016/j.fertnstert.2020.01.001.(https://www.sciencedirect.com/science/article/pii/S0015028220300017)*

10. *Gregg, A.R., Aarabi, M., Klugman, S. et al. Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: a practice resource of the American College of Medical Genetics and Genomics (ACMG). Genet Med 23, 1793–1806 (2021). https://doi.org/10.1038/s41436-021-01203-z*

11. *Phadke SR, Puri RD, Ranganath P. Prenatal screening for genetic disorders: Suggested guidelines for the Indian Scenario. Indian J Med Res. 2017 Dec;146(6):689-699. doi: 10.4103/ijmr.IJMR_1788_15. PMID: 29664026; PMCID: PMC5926339.*

12. *Allyse M, Minear MA, Berson E, Sridhar S, Rote M, Hung A, et al. Noninvasive prenatal testing: a review of international implementation and challenges. Int J Womens Health. 2015;7:113–26*

IMPROVING GLYCEMIC INSIGHT IN PCOS: NEW TOOL IN THE ARMAMENTARIUM

Gunjan Sharma
Resident
Pikee Saxena
Director Professor
Department of Obstetrics and Gynecology,
Lady Hardinge Medical College & SSKH, New Delhi

Polycystic ovary syndrome (PCOS) is the leading cause of infertility. The reported incidence is as high as 26% worldwide1. PCOS is not only about the ovaries as its name signifies, it is a "multisystem reproductive metabolic disorder" and is quietly related to body's capability to manage glucose and insulin effectually, with up to 70% of women having insulin resistance2 in PCOS.

PCOS is an imbalance in a woman's hormone levels and frequently includes symptoms of menstrual irregularity, obesity (80% prevalence2 in PCOS), hirsutism, infertility, hyperandrogenemia, increased insulin resistance (hyperinsulinemia), and multiple immature antral follicles in the ovaries. The exact cause of PCOS is not well known, but a combination of lifestyle and genetic factors is likely to be involved in the etiology. PCOS puts women at major risk for developing Type 2 diabetes, with more than half of women3 with PCOS developing Type 2 diabetes by the time they reach 40 years of age.

Research from 2017 suggests that people with PCOS are four times more likely to develop type 2 diabetes than similar peers without the disorder4

A study of around 8,000 females found that those with PCOS had a much higher risk of developing gestational or type 2 diabetes5. The researchers note that this finding was independent of body mass.

It's important to note that PCOS is a prediabetic condition and these women have high risk of developing gestational diabetes during pregnancy.

Insulin and glucose regulation are directly influenced by diet and lifestyle changes, various research papers have been done to demonstrate their impact on PCOS and the results are very reassuring.

This article describes the opportunities to use new technological innovations like continuous glucose monitoring (CGM) to guide daily food choices and exercise interventions that can optimize health in order to improve PCOS.

PCOS and insulin resistance: bidirectional relationship between androgens and insulin

Insulin is a vital hormone in keeping blood glucose

levels under control. When carbohydrates are eaten, insulin is secreted from the pancreas to remove glucose from bloodstream and into the cells. Excess sugar intake, lack of physical activity, poor sleep, environmental toxins, chronic stress, and genetic factors can all lead to conditions of high glucose and insulin which over a period of time make the cells "numb" to the effects of insulin, this process is called as insulin resistance6. When this happens, less glucose is able to get into cells, hence more insulin is produced to help remove the excess glucose from the bloodstream. When this process goes on for longer period of time, it can develop into prediabetes and then ultimately into Type 2 diabetes.

Figure 1. Pathophysiology of PCOS

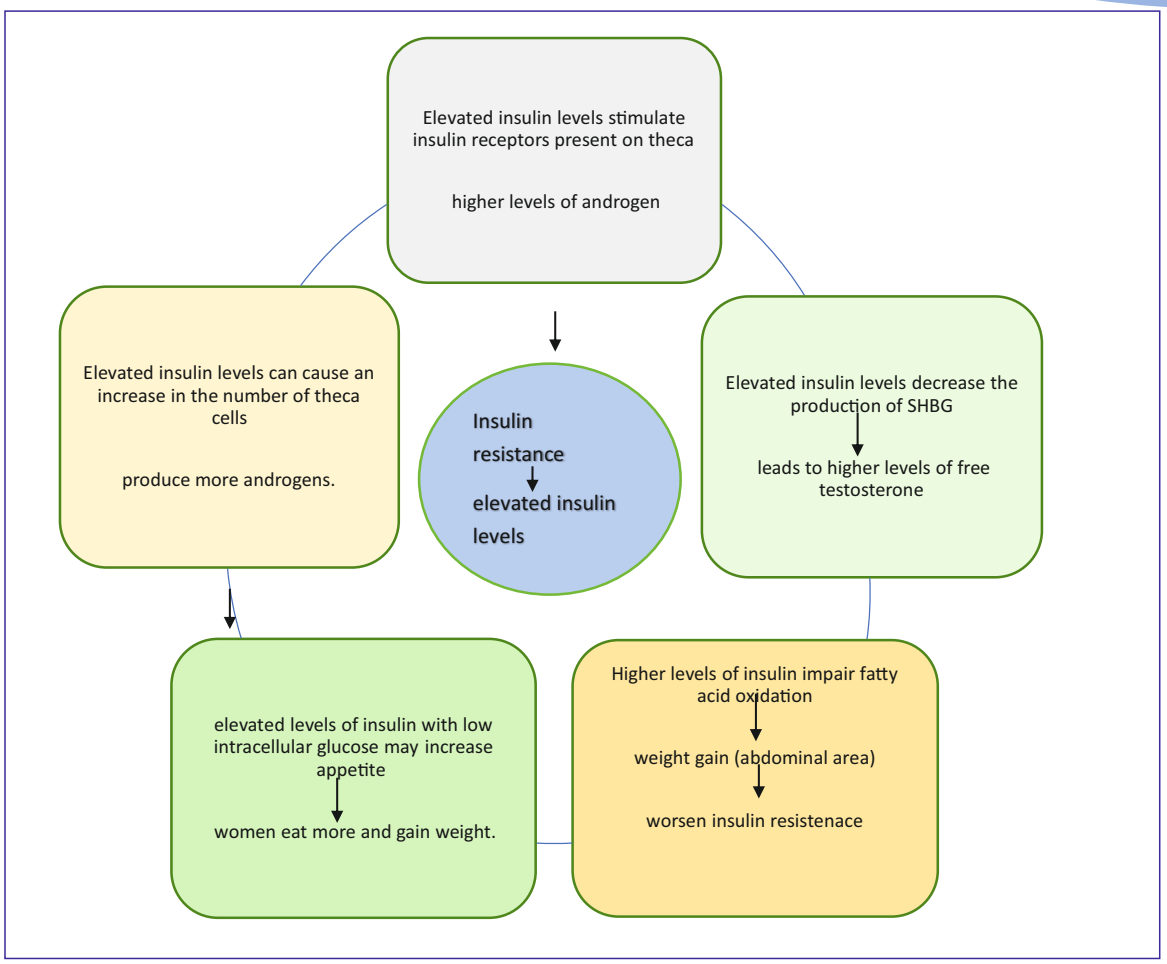
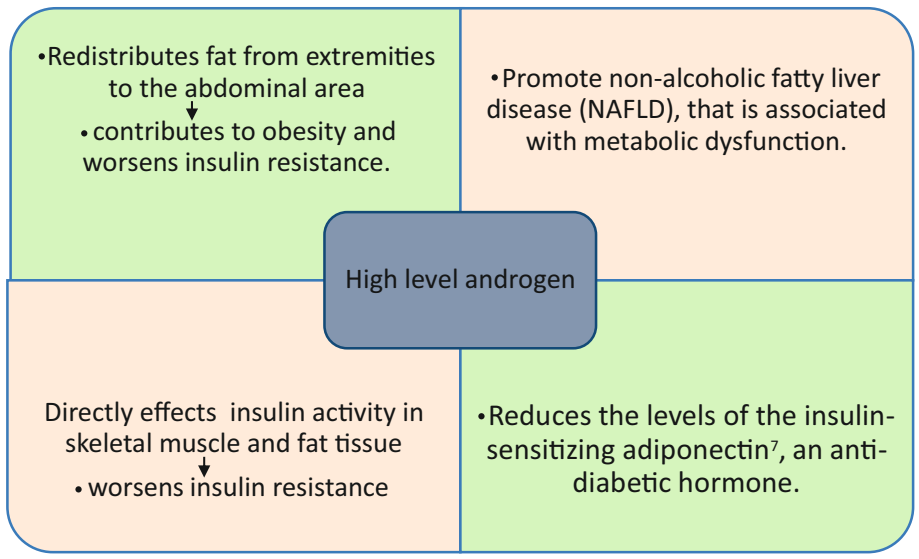


Figure 2. Manifestations of hyperandrogenemia



Role of diet and lifestyle change in tackling PCOS

As PCOS along with fertility issues, also puts women at a risk of developing type 2 DM and gestational diabetes mellitus later in life, hence breaking this vicious cycle of insulin resistance at earlier stage becomes extremely important. Research has shown that lifestyle and dietary factors can play an important role by contributing to weight loss and increasing insulin sensitivity. Although there is no such single diet for PCOS that will treat the condition, but various evidences suggest that use of low glycaemic index8 (LGI) and ketogenic diets may be fruitful.

The glycaemic index of a food refers to how much it raises blood glucose levels after consumption. Low glycaemic index8 foods include beans, legumes, non-starchy vegetables, certain fruits, nuts, seeds, tofu, and animal protein. In general, foods with higher fibre also have a lower glycaemic index because fibre slows digestion and makes some carbohydrates less digestible.

Several studies report that an LGI diet may be beneficial for women with PCOS.

• A study9 was done over 24 weeks in 21 women with PCOS. They consumed their usual diet for first 12 weeks after that they were started on LGI diet that was calorically equivalent to the diet they have consumed during the first 12 weeks of the study. After 12 weeks on the LGI diet, researchers found that insulin resistance had decreased significantly.

• A review10 from 2017 that included seven research papers studying the effect of low carb diets on fertility outcomes illustrated improvement in fertility with low carb diets. The authors inferred that "there is convincing evidence that reducing carbohydrate load can reduce circulating insulin levels, improve hormonal imbalance and result in a resumption of ovulation to improve pregnancy rates. Numerous studies have shown that low carbohydrate diets not only elicit fast and significant weight loss but also reduce serum insulin, consequently improving insulin sensitivity."

Same food may have very different effects on the glucose levels in different individuals. Hence, generalised dietary modifications may not be proved beneficial in all women. The evidences are continuing to emerge from various researches that promotes the benefit of ketogenic, low-carbohydrate, and low glycaemic diets in women with PCOS but these diets can be difficult to implement, maintain and monitor.

Traditional self-monitoring of blood glucose by glucometer and venous blood sugar testing from the laboratories are the conventional methods for monitoring glycaemic profile. The disadvantages of these methods is that they give a snapshot of glucose level at that particular moment and not a trend or continuous profile, they are painful, inconvenient, require lot of self-motivation to perform several times over a day. They do not pick up the exact duration of hypoglycaemia or hyperglycaemia events. They also fail to predict how much glucose levels rise after consuming different food items which may help in training and adjusting diet and exercise.

These limitations can now be overcome by measuring continuous glucose profile by use of convenient and handy, flash glucose monitoring system, which is a new landmark technological innovation in this field.

How can flash glucose monitoring (FGM) help in PCOS?

Flash glucose monitoring11 (FGM) may provide a more precise and individualized approach in formulating a diet that aids in keeping blood glucose levels stable and insulin levels low in women with PCOS. It is a novel method of continuous glucose monitoring. FGM comprises of a sensor which is applied on left upper arm by an adhesive and a separate touchscreen reader device is used which transmits instantaneous glucose level and 24 hours' trend graph (Picture 1,2,3). It measures glucose level of interstitial fluid surrounding the subcutaneous tissue cells. Glucose levels are recorded on the device every 15 minutes and changes in glycaemic trends such as hyperglycaemia and hypoglycaemia can be assessed accurately. This method can not only monitor blood glucose continuously, but also can display blood glucose fluctuations. It measures 96 glucose values per day and one device can be used for 14 days. FGM is being manufactured by Abbott Diabetes care by the name of Freestyle Libre Pro. It was approved by FDA for ambulatory glucose profile monitoring on 23 July, 2018.

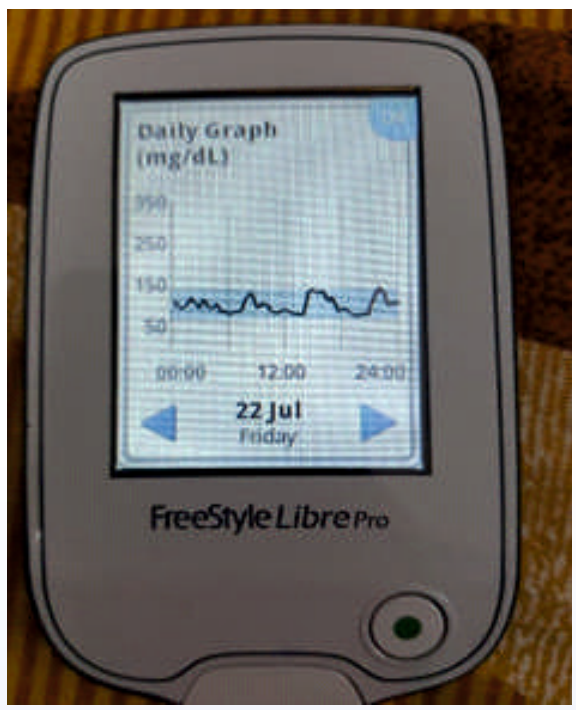
It allows for the measurement of blood glucose levels in real-time, providing instant and individualized feedback on dietary and lifestyle choices and also helps in monitoring the impact of the choices that patients have made on processes that drive PCOS symptoms. Hence it makes FGM, an extremely beneficial tool in optimizing diet and empowering patients to take charge of the modifiable aspects of PCOS.

FGM provides a more detailed account of daily glucose pattern, hence it may also help in recognising women with PCOS who have insulin resistance earlier than the other testing methods. It has been observed that there is a significant glycaemic variability in women with PCOS (Picture 4) where hypoglycaemic periods are shown to go below 70mg/dl which are marked in red and hyperglycaemia events above 140mg/dl are highlighted in yellow for patient's understanding. Glycaemic variation or fluctuation is within normal range in non PCOS patient's graph (Picture 4). The hypo and hyperglycaemia limits can be changed as per physician's advice. As shown in Picture 4, the graph also gives average glucose values over 24 hours, estimated HbA1c over 14 days, percentage of times the patient had hypo or hyperglycaemia as well as percentage of time she had glucose values within range. Exact blood glucose values every 15 minutes can also be seen on the computer. If the patient maintains a detailed food and exercise diary she can be taught about the trends of glycaemic excursions after different food items during day time and also at night which would be otherwise missed.

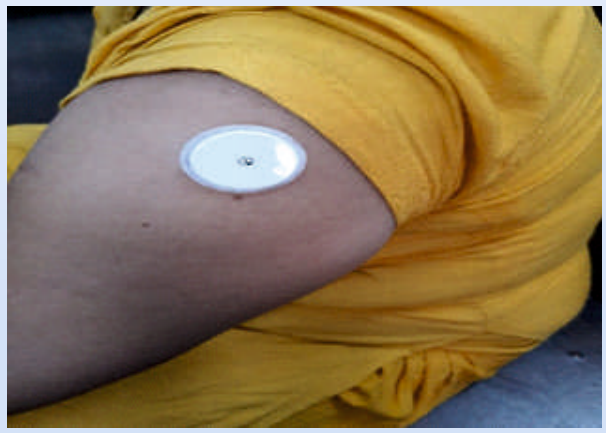
FGM is indeed proving to be a very useful training and educational tool when used under guidance. In fact, it is increasingly becoming popular among health conscious normoglycemic individuals for keeping a check over their dietary patterns.

Tao M et al12 conducted a study in 2011 on Forty-five women with PCOS and normal glucose tolerance and 45 healthy, age-matched women (control group). They underwent a 3-day period of blood glucose (BG) monitoring using the CGM system. Various parameters like mean level of 24-hour BG value (MBG), standard deviation of BG (SDBG) and mean amplitude of glycaemic excursion (MAGE), postprandial glycaemic excursions(PPGEs) were measured. Based on CGM, the times to peak glucose of patients with PCOS after 3 meals were higher than the control group (42 ± 18 min vs 32 ± 12 min, 54 ± 25 min vs 39 ± 18 min, and 45 ± 16 min vs 38 ± 16 min, respectively; $P < 0.05$), and the amplitude of PPGEs after breakfast was higher than the control group ($P < 0.05$). It was concluded that women with PCOS and normal glucose tolerance have changes in PPGEs. Continuous glucose monitoring can detect alterations in a comprehensive and sensitive way.

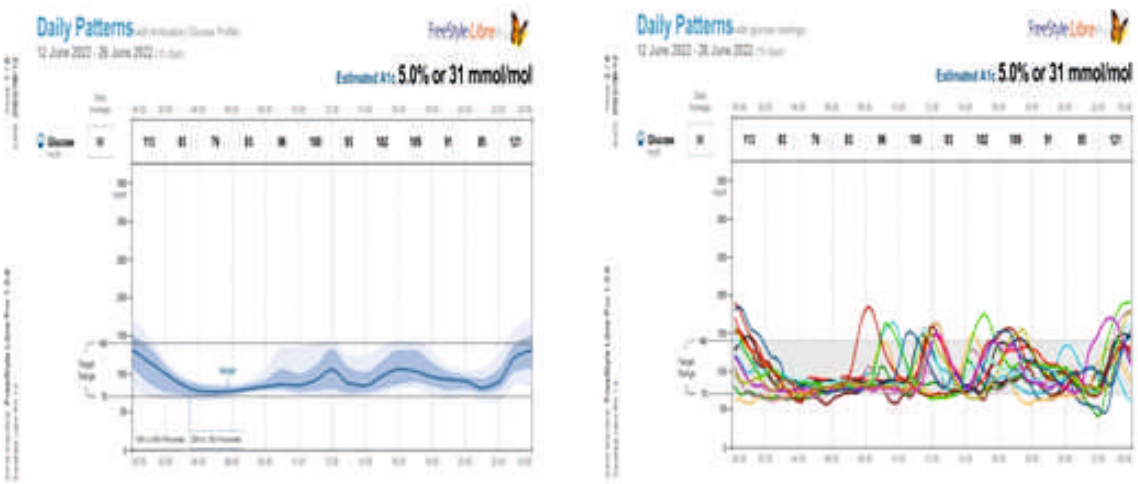
PICTURE 1 :FreeStyle LibrePro flash glucose monitoring system and FGM Reader



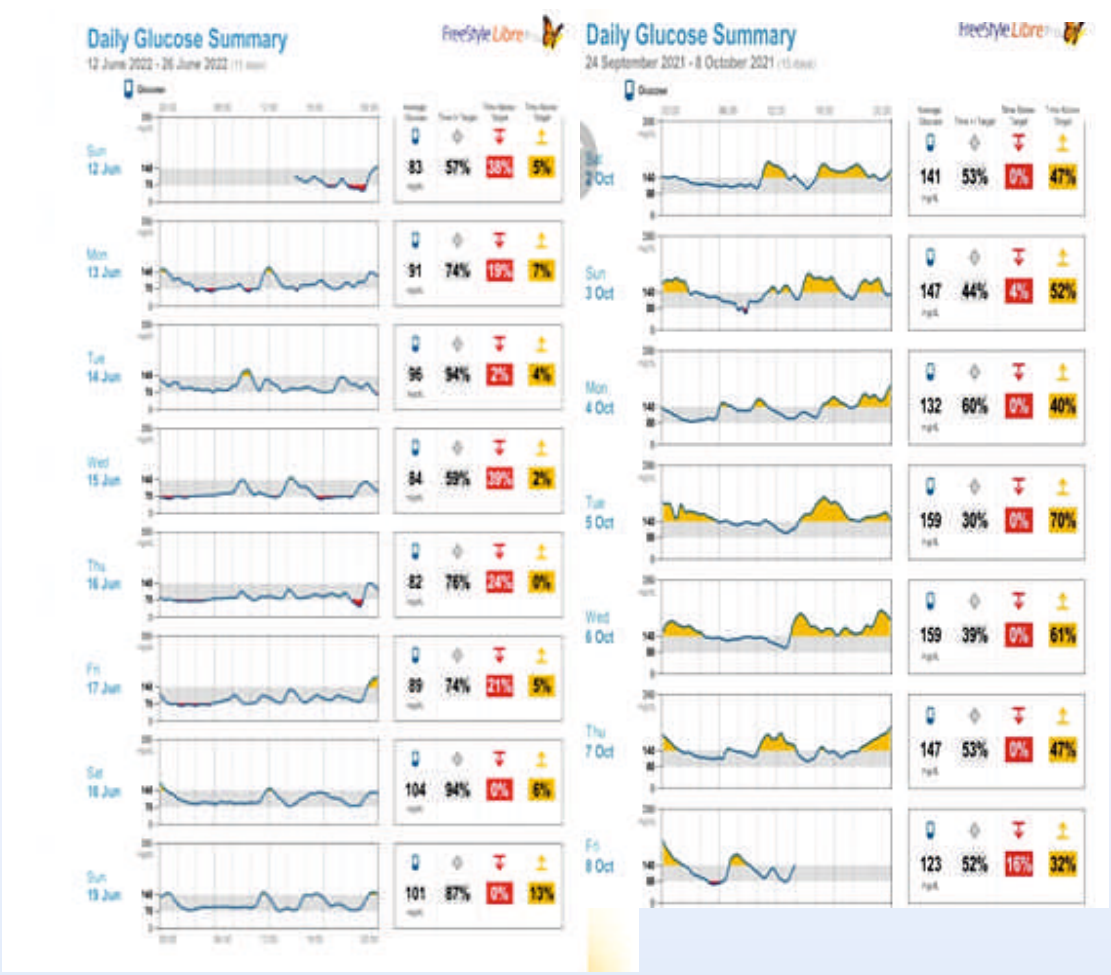
PICTURE 2 :FGM sensor applied on patient's arm



PICTURE 3 : FGM graph showing daily pattern and estimated HbA1c



PICTURE 4: First picture showing glucose fluctuations of non PCOS women and second picture showing glucose fluctuations of PCOS women with insulin resistance



Conclusion

PCOS is a prediabetic condition, it involves hormonal imbalances that involve both the reproductive and metabolic systems. The exact causes are likely multifaceted, dietary and lifestyle factors play an important role in disease severity, and new tools may help in alleviating these symptoms.

FGM can guide individualized dietary and lifestyle choices to minimize and prevent glucose fluctuations that promote insulin secretion.

The vicious cycle of elevated androgens and insulin resistance in PCOS can be interrupted by maintaining stable blood glucose and insulin levels to curtail the development of insulin resistance and its associated negative health consequences. FGM helps in accomplishing this by equipping individuals with the necessary tools to track the foods they consume and see which ones have a low glycaemic index for them and also educating them regarding their glucose excursions and future risk of developing diabetes in later life. By having this, personalized and graphical information, smart food choices and lifestyle changes can be made that will have long-lasting, positive effects on both PCOS symptoms and overall health.

References:

1. Bharathi RV, Swetha S, Neerajaa J, Madhavica JV, Janani DM, Rekha SN, Ramya S, Usha B. An epidemiological survey: Effect of predisposing factors for PCOS in Indian urban and rural population. Middle East Fertility Society Journal. 2017 Dec 1;22(4):313-6

2. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocrine reviews. 2012 Dec 1;33(6):981-1030.

3. https://www.cdc.gov/diabetes/basics/pcos.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fdiabetes%2Flibrary%2Fspotlights%2Fpcos.html

4. Rubin KH, Glintborg D, Nybo M, Abrahamsen B, Andersen M. Development and risk factors of type 2 diabetes in a nationwide population of women with polycystic ovary syndrome. The Journal of Clinical Endocrinology & Metabolism. 2017 Oct 1;102(10):3848-57.

5. Joham AE, Ranasinha S, Zoungas S, Moran L, Teede HJ. Gestational diabetes and type 2 diabetes in reproductive-aged women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2014 Mar 1;99(3):E447-52.

6. https://www.levelshealth.com/blog/what-causes-insulin-resistance-glucose-levels

7. Nishizawa H, Shimomura I, Kishida K, Maeda N, Kuriyama H, Nagaretani H, Matsuda M, Kondo H, Furuyama N, Kihara S, Nakamura T. Androgens decrease plasma adiponectin, an insulin-sensitizing adipocyte-derived protein. Diabetes. 2002 Sep 1;51(9):2734-41.

8. Coyle D, Kuballa J. A Beginner's Guide to the Low-Glycemic Diet.

9. Barr S, Reeves S, Sharp K, Jeanes YM. An isocaloric low glycemic index diet improves insulin sensitivity in women with polycystic ovary syndrome. Journal of the Academy of Nutrition and Dietetics. 2013 Nov 1;113(11):1523-31.

10. McGrice M, Porter J. The effect of low carbohydrate diets on fertility hormones and outcomes in overweight and obese women: A systematic review. Nutrients. 2017 Feb 27;9(3):204.

11. Freestyle Libre flash glucose monitoring system. Online [Cited 2015 May 30]. Available from URL:http://www.freestylelibre.co.uk/freestylelibre-reader-kit-mmoll-en-gb.html

12. Tao M, Zhou J, Zhu J, Lu W, Jia W. Continuous glucose monitoring reveals abnormal features of postprandial glycemic excursions in women with polycystic ovarian syndrome. Postgraduate medicine. 2011 Mar 1;123(2):185-90.

INVITED ARTICLES

Effect of Yoga and Counselling on the success of IUI/ IVF/ ET Cycles

Dr. Sudha Prasad and Dr. Saumya Prasad
Matritava Advanced IVF & Training Centre, Delhi

Background:

Assisted reproduction is a promising procedure which is carried out in a controlled body parameter in women diagnosed with infertility due to known and unknown reasons (1). IUI-IVF-ET is a process performed routinely all around the world but still its success marks differently for different women.

Other than employing highly specialized medical procedures and sophisticated technology the positive outcome depends upon various parameters (2), which need to be worked in a synchronized manner till successful birth in assisted conception cycles.

The reach to avail the facility of IVF treatment is limited to such infertile couples who belong to lower economical strata. The limitations may be responsible for long standing infertility which itself causes various social, medical, and psychological problems. There is tremendous increase of stress level in these women. The different stress levels may affect the management of clinical outcome in such women (3).

In present RCT, 415 women were enrolled as per inclusion and exclusion criteria. Women were randomly assigned to one of the two groups viz; Yoga & counseling Group and Non-Yoga & non-counseling group after complete worked-up for IVF or IUI as per their treatment of choice. The stress management was based on the different movement and postures (Kriyas and Asana) and counseling, simultaneously.

The Yoga applications comprised; Kriyas or cleaning processes (Ghrit neti, Sutra neti, Jal neti, Jal paan, Dugdha paan), Asanas or postural patterns (Jeevan tatva, Serpasana, Naukasana and Half-sarvangasana), Pranayama or regulated breathing (Anulom-Vilome) and Yogic Relaxation in Shavasana(4).

Supportive counseling by psychological tools based on the concepts of Yoga included; Cornell Medical Index (CMI) , Amritsar Depressive Inventory (ADI)(Singh et al 1974), Hamilton's Rating Scales for Anxiety (HAM-A) (Hamilton, 1959), Hamilton's Rating Scale for Depression (HAM-D) (Hamilton, 1979), Presumptive stressful life events scale (PSLES) (Singh et al 1984), Sinha's Comprehensive Anxiety Test (SCAT), Fertility and Quality of Life Questionnaire (FERTIQOL)(5,6,7,8,9,10).

Demographic data was compiled and analysed.

Age of women in study group was ranged between 21 to 38 years. The mean age of the women was 30.32± 4.4 (P > 0.5) and was found non-significant. The duration of infertility among these women was from <5 years to >14 years.

Being the referral hospital women reaches to our centre quite late. The overall duration of infertility was from 2 to 21 years. The mean duration of infertility was 7.38 ± 4.43 years in Yoga group and 7.77 ± 3.91 years in non-Yoga group (P = 0.019) and was found statistically significant.

The effects of interventions (Yoga and counseling), the uterine artery blood flow parameters were measured 2D Doppler ultrasonography before starting the investigations (firstly in early follicular phase called as base line parameters) and was repeated on the day of trigger which was done to achieve the final maturity of oocytes in IUI or IVF treatment cycles.

The uterine artery Doppler indices indicated better uterine perfusion in Yoga group compared to non-Yoga group. The pulsatility index (PI), measured on day of early follicular phase (1.99±1.01), as well as that measured on the day of hCG injection (2±1.03), was found to be significantly better in Yoga group, (P = 0.022 and 0.025 respectively) than non-Yoga group (1.76±0.94 and 1.75±1.01). The mean PI (1.92 ± 1.12) value in women who became pregnant in Yoga group was found to be significantly higher than in non-Yoga group (1.35± 0.89) P= 0.015 on contrary to our results, Cacciatore et al (1996) observed that PI and RI were lower in conception (2.45 +/- 0.54 and 0.85 +/- 0.04) as compared to non-conception cycles (2.66 +/- 0.39 and 0.87 +/- 0.04) (11).

Among 285 women who underwent IVF-ET procedure, a total of 162 women in yoga group, 77 (47.5%) women achieved successful pregnancies. whereas only 31 (25.2%) women were found to have positive pregnancy outcome among 123 women of non-yoga group. This difference was found to be statistically significant (p=0.005*)

Similarly, women who underwent IUI cycles, Yoga group (27/130) and non-Yoga group (103/130), achieved successful pregnancy outcome in 04 (14.8%) among Yoga group and 09 (8.7%) women in non-Yoga group. The difference in the success rate was comparable and was found statistically significant difference (p=0.004*).

The clinical outcomes in of Yoga group (N=189) and non-Yoga group (N=226) were statistically significant (P= 0.005).

The group of women who underwent, counseling and yoga-based stress management before IVF procedure, experienced highly improved pregnancy outcome. Pregnancy rate in Yoga group was higher (77/162, 47.5% and 4/27; 14.8% in IVF & IUI treatment cycles respectively) than non-Yoga group (31/123, 25.2% and 9/103; 8.7% in IVF & IUI treatment cycles respectively), P=<0.005 as shown in table 1.

Table 1. Distribution of women according to Outcome of Pregnancy

Type of Cycle (N)		Pregnancy Outcome		*P* value
		Positive	Negative	
IUI (N=130)	Yoga 27(20.7%)	04 (14.8%)	23 (85.2%)	0.004%
	Non-Yoga 103(79.3%)	09 (8.7%)	94 (91.3%)	
IVF (N=285)	Yoga 162 (56.8%)	77 (47.5%)	85 (523.5%)	*0.005***
	Non-Yoga 123(43.2%)	31 (25.2%)	92 (74.8%)	
Total (N= 415)		121	294	

An attempt was made to standardize the mandatory number of Yoga sessions (minimum prerequisite as cut-off) required before exposure of the patients to IVF/IUI treatment cycles and the implementation of Yoga and counseling to achieve higher pregnancy rates as routine practice in clinical settings. The Yoga sessions were sub-grouped as 3-15 sessions, 16-30 sessions and >30 sessions shown in table 2.

Table 2. Effect of the number of yoga sessions on pregnancy outcome

Number of Yoga sessions attended	Pregnancy Outcome		Total	P value
	Positive	Negative		
<3	0	13(11.3)	13(6.5)	<0.005
3-15	24(28.5)	64(55.6)	88(44.2)	
16-30	27(32.1)	18(15.6)	45(22.6)	
>30	33(39.28)	20(17.39)	53(26.6)	
Total	84(100)	115(100)	199(100)	

Fig.3: ROC curve analysis of Yoga Sessions

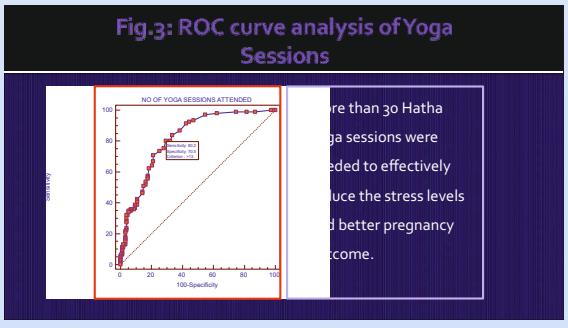


Table 3: Pre and post assessment comparison- study and control groups (205 vs. 203)

Psychological Assessment	Pre Assessment (Mean± S/D)	Post Assessment (Mean± S/D)	P value
ADI	8.3±7.43	5.98±6.97	<0.0005
HAM-A	11.75±8.39	8.11±6.48	<0.0005
HAM-D	11.45±7.05	8.16±5.5	<0.0005
SCAT	23.53±21.08	15.48±18.92	<0.0005
CMI	23.56±21.8	14.37±15.9	<0.0005
Psychological Assessment	**Pre Assessment (Mean± S/D)**	**Post Assessment (Mean± S/D)**	**P value**
ADI	8.08±8.37	5.87±7.23	0.059
HAM-A	10.66±7.34	10.47±7.3	0.893
HAM-D	11.68±6.9	10.68±6.3	0.384
SCAT	20.36±22.5	13.92±17.48	0.035
CMI	20.29±16.85	14.16±14.92	0.006
Fertiqol	53.18±15.95	57.09±13.38	0.189

Post assessment stress levels significantly reduced in both study and control groups
Reduction much more significant in study group

Table 4: Pre & Post assessment in pregnant women

Psychological Assessment STUDY	Pre Assessment (Mean± S/D)	Post Assessment (Mean± S/D)	P value Study
ADI	7.9±7.43	4.49±5.78	<0.0005
HAM-A	11.26±7.46	6.98±5.79	<0.0005
HAM-D	10.8±6.86	6.85±4.1	<0.0005
SCAT	21.07±18.51	14.06±17.09	<0.0005
CMI	23.09±22.35	14.04±15.27	<0.0005
Fertiqol	54.05±12.48	58.75±14.54	0.003
Psychological Assessment CONTROL	**Pre Assessment (Mean± S/D)**	**Post Assessment (Mean± S/D)**	**P value Control**
ADI	8.08±8.37	5.87±7.23	0.059
HAM-A	10.66±7.34	10.47±7.3	0.893
HAM-D	11.68±6.9	10.68±6.3	0.384
SCAT	20.36±22.5	13.92±17.48	0.035
CMI	20.29±16.85	14.16±14.92	0.006
Fertiqol	53.18±15.95	57.09±13.38	0.189

The post test assessments were more significantly lower in pregnant women in study group compared to control group

It has been observed women who attended >30 sessions of Yoga showed highest success rate in terms of clinical pregnancy outcome (P=0.005*).

Comparison of scores at recruitment and after treatment intervention in the study group showed a significant reduction in depression, anxiety, as well as specific stress related to infertility and its treatment as shown in Table 3.

Studies in India as well as abroad have reported that a high percentage of couples discontinued the treatment due to psychological stress (12), whereas we found the Yoga and non-Yoga group showed reduction in scores and found statically highly significant.

Women who achieved their successful pregnancies showed a significant reduction in anxiety level as reflected in SCAT only, which was not reflected in HAM-A. Similarly, a slight increase in FERTIQOL indicate an improvement in overall quality of life. Hence, ooverall, there was a trend towards better emotional health. However, effect was not very strong in non-Yoga group.

Boivin and Schmidt, 2005 (13) reported that fertility problem stress (infertility-induced stress) was associated with a poorer treatment outcome in women and men, with the effect significantly more pronounced for women whereas in our study infertility related psychological complication (depression, anxiety, fatigue and insomnia) and stress was reduced immensely after successfully managed by applying supportive counseling with psychological tools based on the concepts and art of Yoga.

The treatment intervention, both standard treatment as well as the yoga-based stress management was helpful at the psychological level also. However, the magnitude of psychological improvement was more in the study group, with highly significant reduction in anxiety, depression and an enhanced overall quality of life. All the cases with positive pregnancy outcome showed significant reduction in anxiety, depression and infertility related stress regardless of whether they were in the study or the control group. Again, the positive emotional change was greater in the study group. This was seen in the magnitude as well as consistency of change on the variety of outcome measures. The data here indicates that the psychological stress reduction is enhanced by the yoga-based stress management. Thus, psychological screening and Yoga should be a definitive part of infertility management.

The counselling and group Yoga sessions were also attended by women even after conception which led to significant reduction in anxiety, depression, Infertility related stress, the positive emotional change with improved family relations to achieve their successful pregnancies.

Combined therapy may be advocated for relieving both; infertility related stress and stress related infertility. It should be considered as paramount aspect before approaching the problem of infertility and enrolment and worked up of any infertile women for assisted reproduction.

Acknowledgement: Funded by ICMR while at MAMC.

References:

1. Berg BJ, & Wilson JF, Psychiatric morbidity in the infertile population: a reconceptualization. Fertility and Sterility 1990: 53, 654–661.

2. Menning BE, The emotional needs of infertile couples. Fertility and Sterility1980: 34, 313–319.

3. Beaurepaire J, Jones M, Thiering P, Saunders D, & Tennant C, Psychosocial adjustment to infertility and its treatment: male and female responses at different stages of IVF/ET treatment. Journal of Psychosomatic Research 1994: 38, 229–240.

4. Grover, P.; Varma, V.K.; Verma, S.K.; Pershad, DRole of Yoga in the treatment of Psychoneurosis –Current status and future indications. Indian Jl. Psychiatry. 1994; 30:153-162.

5. Hamilton M, The assessment of anxiety states by rating. The British Journal of Medical Psychology 1959:32, 50–55.

6. Hamilton M, A rating scale for depression. Journal of Neurology 1960:23, 56–62.

7. Singh G, Kaur D, & Kaur H, Presumptive stressful life events scale (PSLES) - a new stressful life events scale for use in India. Indian Journal of Psychiatry 1984:26, 107–114.

8. Wig NN, Pershad D, Cornell Medical Index Health Questionnaire-Hindi translation. Psychiatry Dept. PGIMER, Chandigarh 1978.

9. Singh G, Verma HC, Verma RS, Kaur H: A new Depressive Inventory-Amritsar Depressinve Inventory.Indian Jl. Psychiatry 1974:16. 183-186.

10. Sinha AKP, & Sinha LNK, Manual for Sinha's Comprehensive Anxiety Test (SCAT). National Psychological Corporation: Agra 1995.

11. Cacciatore B, Simberg N, Fusaro P, et al. Transvaginal Doppler study of uterine artery blood flow in in vitro fertilization embryo transfer cycles. Fert Steril. 1996; 66: 130–134.

12. Olivius C, Friden B, Borg G, & Bergh C, Why do couples discontinue in vitro fertilization treatment? A cohort study. Fertility and Sterility 2004: 81, 258–261.

13. Boivin J, & Schmidt L, Infertility-related stress in men and women predicts treatment outcome 1 year later. Fertility and Sterility 2005:83, 1745–1752.

IFS SPECIAL INTEREST GROUP (SIG 2022 - 2024)

1. ANDROLOGY

Convenor : Dr M. Venugopal
Co Convenor : Dr Vineet Malhotra
Dr Pranay Ghosh

2. APPLIED GENETICS

Convenor : Dr Deepak Modi
Co Convenor : Dr Sayali Kale Kandhari
Dr Sheetal Jindal

3. COUNSELLING & PATIENT SUPPORT

Convenor : Dr Poonam Nayar
Co Convenor : Dr Puneet Rana Arora
Dr Aanchal Agarwal

4. EARLY PREGNANCY

Convenor : Dr Pikee saxena
Co Convenor : Dr K Aparna Sharma
Dr Renu Tanwar

5. EMBRYOLOGY

Convenor : Dr Gaurav Majumdar
Co Convenor : Dr Gaurav Kant
Dr Dayanidhi Kumar

6. ENDOSCOPY

Convenor : Dr Puneeta Bhardwaj
Co Convenor : Dr Maansi Jain
Dr Priya Bhave Chittawar

7. ENDOMETRIOSIS AWARENESS GROUP

Convenor : Dr Roya Rozati
Co Convenor : Dr Sweta Gupta
Dr Sabina Sanan

8. ENVIRONMENT AND INFERTILITY

Convenor : Dr Renu Misra
Co Convenor : Dr Jayesh S Amin
Dr Anju Mathur

9. FERTILITY PRESERVATION

Convenor : Dr Neena Malhotra
Co Convenor : Dr Reeta Mahey
Dr Pragyanika Gurung

10. HOLISTIC MEDICINE (YOGA, ACUPUNCTURE)

Convenor : Dr Rajvi Mehta
Co Convenor : Dr Ritu Jain
Dr Shalini Chawla Khanna

11. PCOS

Convenor : Dr Bharati Dhorepatil
Co Convenor : Dr Leena Wadhwa
Dr Rhythm Ahuja

12. POR (POOR OVARIAN RESPONSE)

Convenor : Dr Firuza Parikh
Co Convenor : Dr Neeti Tiwari
Dr Nymphea Walecha

13. REPRODUCTIVE ENDOCRINOLOGY

Convenor : Dr Shweta Mittal
Co Convenor : Dr Rajapriya
Dr Himanshu Roy

14. RESEARCH & METHODOLOGY

Convenor : Dr Mohan Kamath
Co Convenor : Dr Ruma Satwik
Dr Garima Kapoor

15. ULTRASOUND

Convenor : Dr Ashok Khurana
Co Convenor : Dr Manjula Handa Virmani
Dr Ladbans Kaur

16. LAWS & ART

Convenor : Dr Rashmi Sharma
Co Convenor : Dr Suneeta Chandra
Dr Parul Garg

17. QUALITY ASSURANCE & CONTROL IN ART

Convenor : Dr Sarabpreet Singh
Co Convenor : Dr Azif Khan
Dr Sarguna Devi

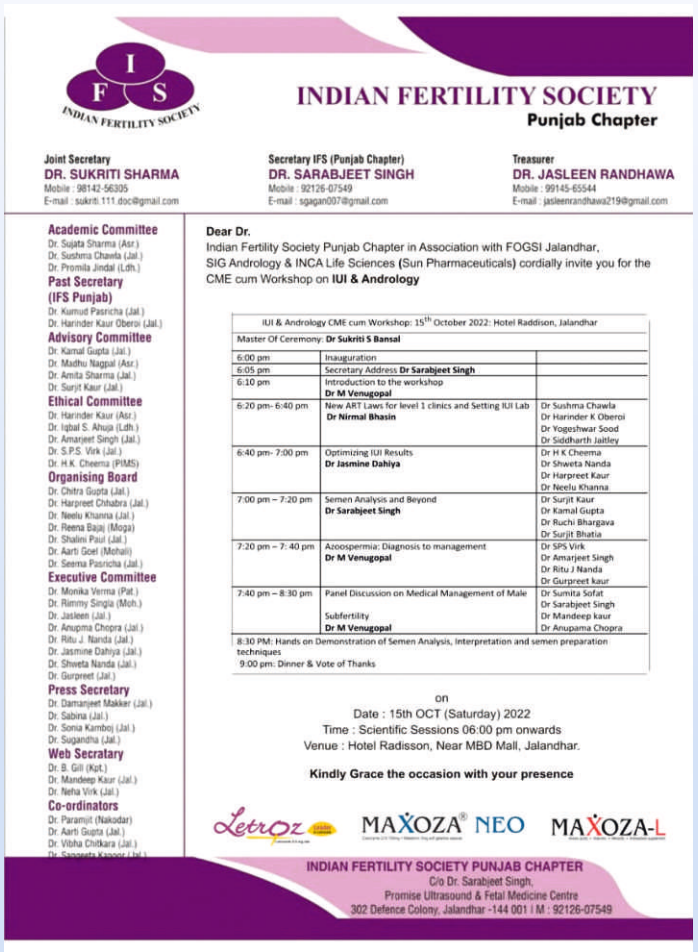
18. PUBLIC AWARENESS

Convenor : Dr Kunjumoideen
Co Convenor : Dr Rupali Bassi
Dr Nitin Lad

IFS ACTIVITIES

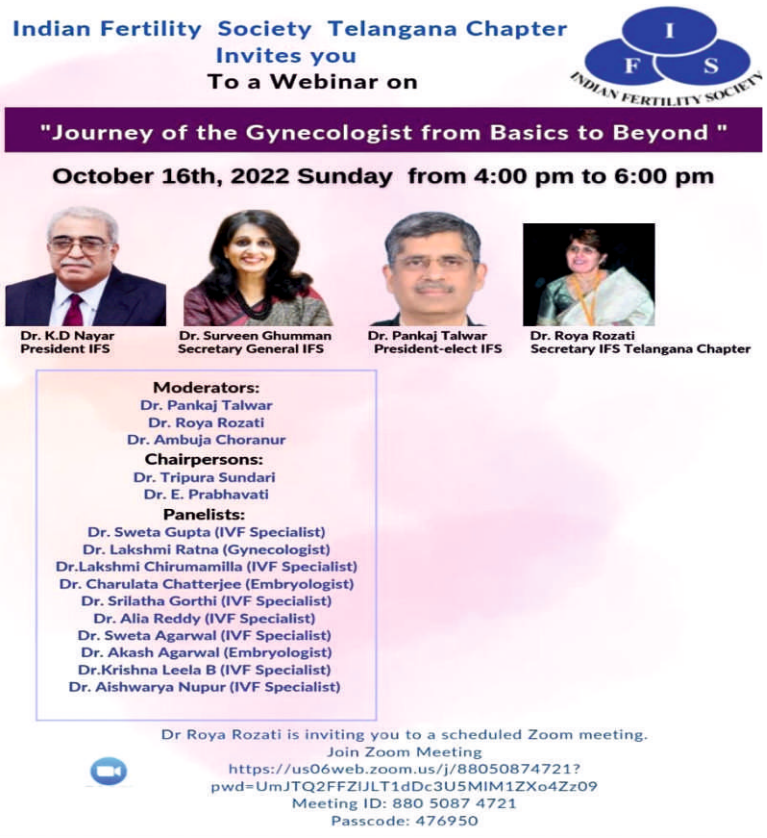
Chapter Activities

IFS RAJASTHAN & SIG ENVIRONMENT AND INFERTILITY ACTIVITY



IFS ACTIVITIES
Chapter Activities

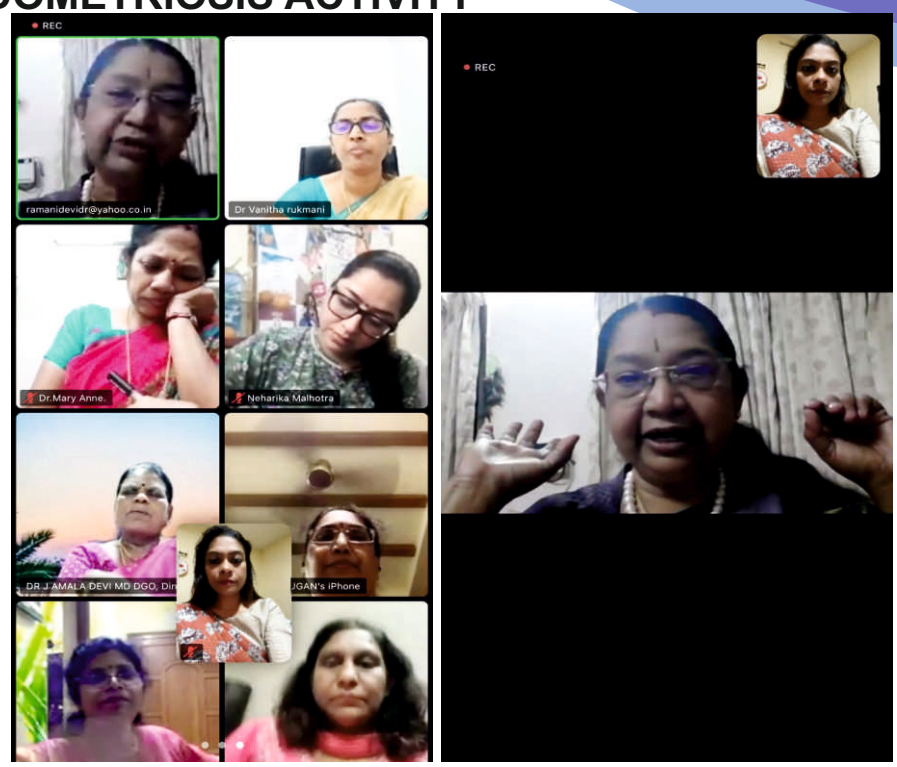
IFS TELANGANA CHAPTER ACTIVITY



IFS MADHYA PRADESH CHAPTER ACTIVITY

IFS ACTIVITIES
Chapter Activities

IFS SOUTH TAMILNADU CHAPTER SIG ENDOMETRIOSIS ACTIVITY

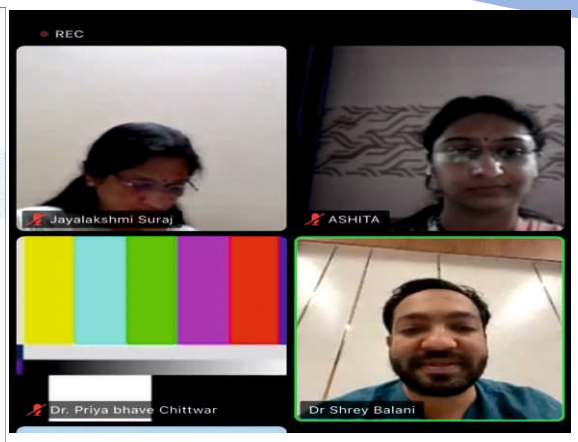


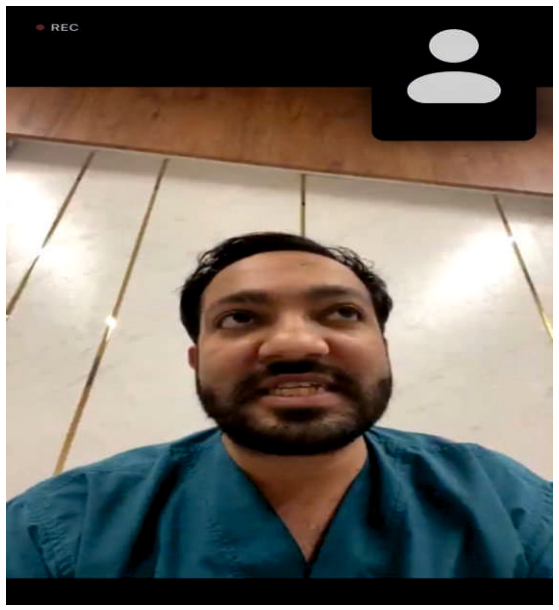
IFS TAMILNADU CHAPTER ACTIVITY

IFS MADHYA PRADESH CHAPTER ACTIVITY

IFS ACTIVITIES
Chapter Activities

IFS MADHYA PRADESH CHAPTER ACTIVITY



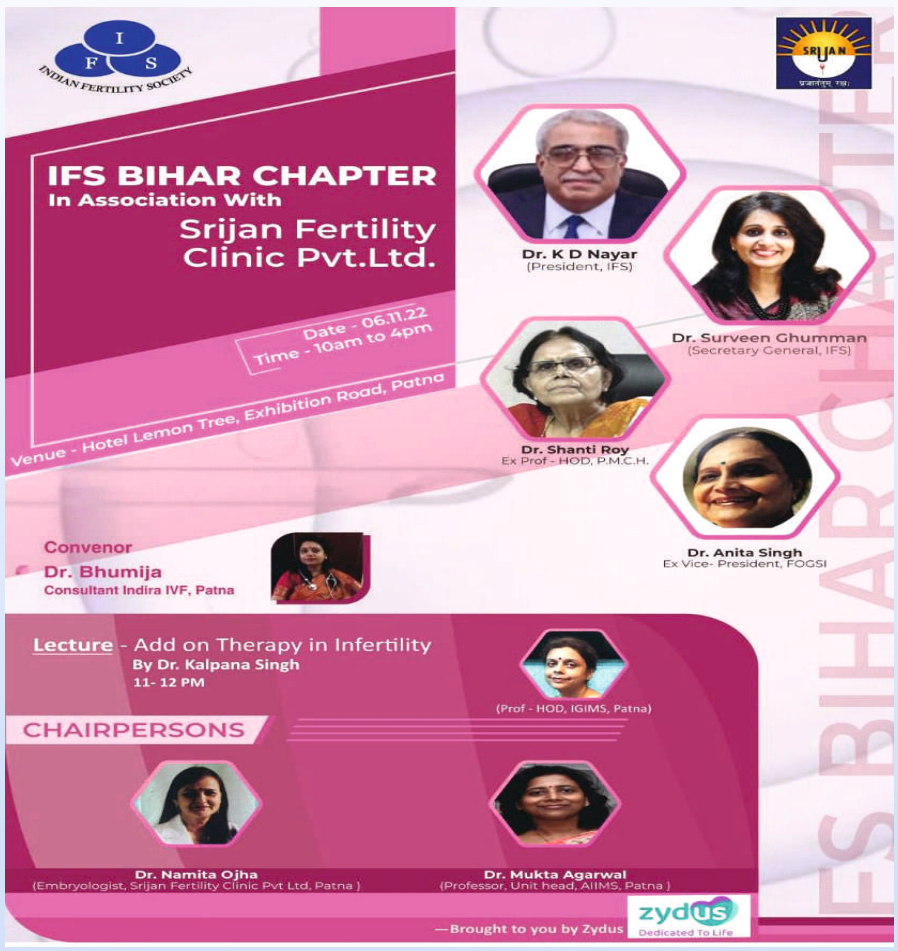


IFS SIG EARLY PREGNANCY ACTIVITY

IFS ACTIVITIES
Chapter Activities

IFS SIG HOLISTIC MEDICINE ACTIVITY

IFS BIHAR CHAPTER ACTIVITY



IFS ACTIVITIES
Chapter Activities

IFS Bihar chapter hosted a conference on 06-11-2022 with talk on ‘Role of adjuvants’ by Dr Kalpana Singh, panel discussion on ‘Troubleshooting in IUI’ with Dr Shivani Sachdev Gaur and Dr Swapnil Singh as moderators and Workshop on Semen preparation by Dr Dayanidhi

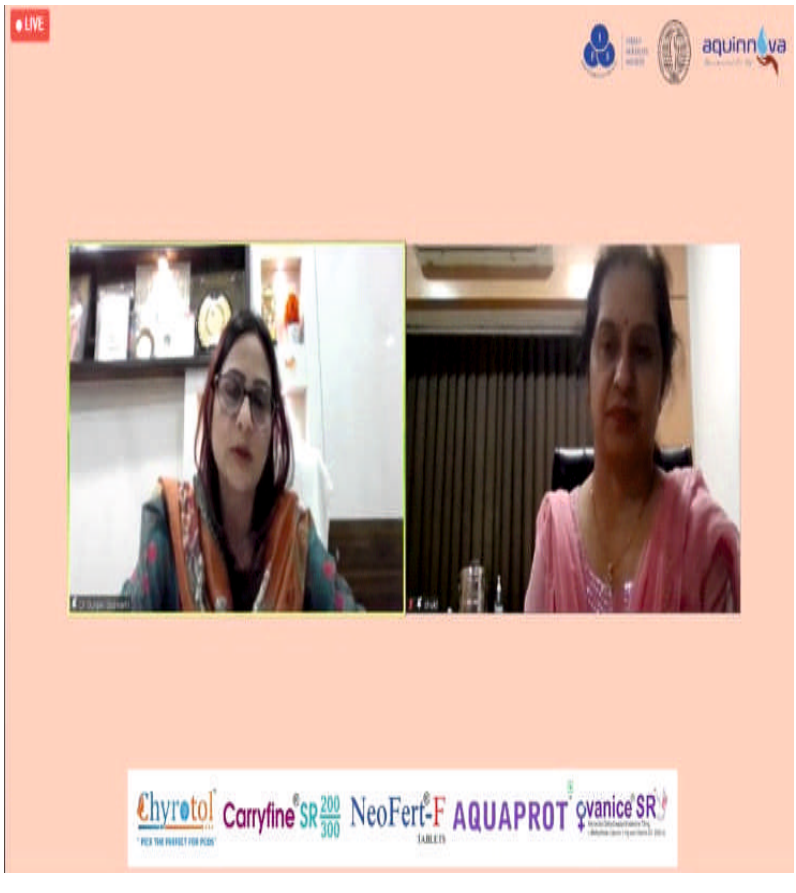
IFS CHHATTISGARH CHAPTER ACTIVITY

IFS ACTIVITIES
Chapter Activities

Scientific session was started with **welcome address by Dr Prakrati Verma IFS CG chapter** secretary session 1 ovarian stimulation optimization. followed by lamp lightening & felicitation of guest speakers. **Dr KD Nayar sir was Chief guest, Dr Pankaj Talwar guest of honor** & other faculties were special guests. Dr KD Nayar sir was given talk on DNA sperm fragmentation .Second session- was **panel discussion on male infertility 3rd session was on mixed topics related to infertility Last session was panel on early pregnancy management Program** was ended with mementos & certificate distribution Vote of thanks given by Dr Anuradha Chaudhary Approx 95 registration was done..

IFS SIG ENDOSCOPY WITH MP CHAPTER ACTIVITY

IFS ACTIVITIES
Chapter Activities



IFS MP chapter and Rewa obstetrics and gynaecology society organised a webinar on 09 Nov2022 from 7pm to 9pmTopic: Role of Hysteroscopy in fertility enhancement SIG : endoscopy Welcome address and introduction of SIG endoscopy presented by Dr Puneeta Bhardwaj. In 2hrs duration all the speakers delivered very informative lectures and covered each and every aspect of Hysteroscopy from theatre set up to management of surgical cases and complications nicely. Speakers were Dr Priya Bhave Chittawar, Dr Kuldeep Jain Dr Mansi Jain Dr Narendra Bhardwaj Dr Puneeta Bhardwaj Dr Dhaval Baxi Dr Padma Shukla Vote of thanks by Dr Gunjan Goswami (master of ceremony)Almost 240 participants attended this webinar ICOG provide 2credit points for this Webinar.

IFS SIG ENDOSCOPY WITH MP CHAPTER ACTIVITY

IFS ACTIVITIES
Chapter Activities

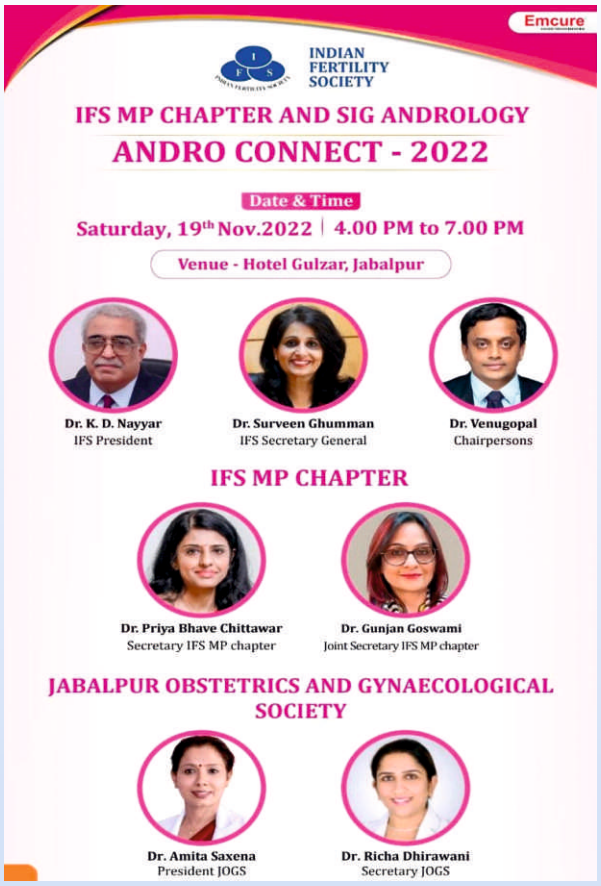
IFS UP EAST CHAPTER ACTIVITY

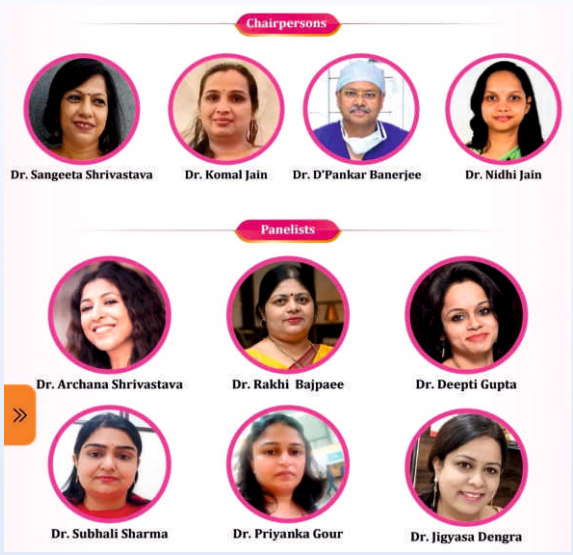
IFS MADHYA PRADESH CHAPTER ACTIVITY

IFS ACTIVITIES
Chapter Activities

IFS MADHYA PRADESH CHAPTER ACTIVITY

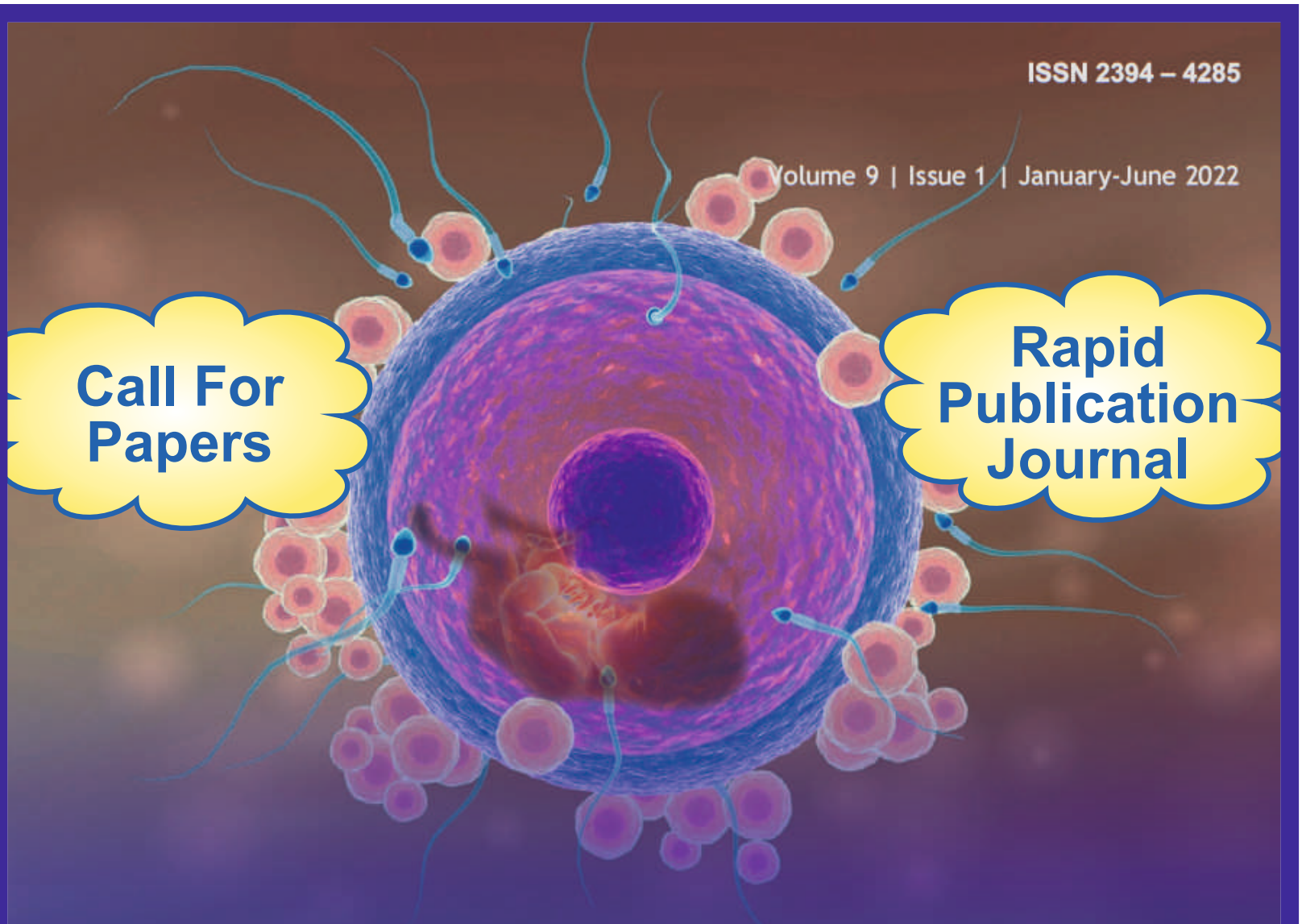
IFS MADHYA PRADESH CHAPTER ACTIVITY





ISSN 2394 – 4285

Volume 9 | Issue 1 | January-June 2022



Call For Papers

Rapid Publication Journal

FERTILITY
Science & Research

Revamped International Editorial Board

Official Publication of Indian Fertility Society

Current Issue

rupalibassi@hotmail.com

www.fertilityscienceresearch.org

Wolters Kluwer

Medknow