2024, Volume 24, May, Issue 01

AOGD BULLETIN

Shared Decision Making - Enhancing Women Emancipation

Theme
Maternal Fetal Medicine:
Delving Deeper into Maternal Fetal Medicine

AOGD SECRETARIAT
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AOGD Bulletin

2024, Volume 24, May, Issue 01

Invited Articles

Publisher/Printer/Editor

Dr. Renuka Malik on Behalf of Assosiation of Obstetrics and Gynaecologists of Delhi

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Message from the President

President

"Great leaders don't set out to be a leader, they set out to make a difference, Its never about the role, its always about the goal"

Dear AOGDians,

It's a matter of great pride and honour that ABVIMS & Dr. RML Hospital is taking over AOGD office for the year 2024-25. First and foremost, I would like to express my heartfelt gratitude to our highly esteemed patrons, advisors, executive committee members, and all my dear colleagues of the association for giving me and my team this wonderful opportunity to serve this prestigious association. The theme for this year is "Shared Decision Making – Enhancing Women Emancipation". The objectives of my team would be threefold - our main goal would be to raise the bar high and imprint AOGD as the best society of FOGSI. Secondly, we will attempt to include the members through various outreach programs, clinical meetings, and forums focusing on skill development. Through the monthly AOGD Bulletin, we will attempt to cover various subspecialties of Obstetrics & Gynaecology- what's new and what's important in currently existing knowledge. Thirdly, the efforts of our team would be directed towards increasing knowledge and awareness regarding the issues of general health of women enabling them to make their own decisions.

Apart from the monthly bulletins, we are planning PG forums, CMEs, hands-on workshops, and various online campaigns along with the annual conference on November 22nd - 24th 2024. In the first issue, we are focusing on Maternal Fetal Medicine, how the expertise of our healthcare professionals has come a long way in improving maternal and fetal outcomes via research, training, and utilizing all the available technological advancement in safeguarding the journey of pregnancy and childbirth. A variety of fetal complications earlier leading to lifelong disability for both the parents and children are now being detected and prevented at an earlier stage consequently.

Looking forward to the upcoming year of wisdom and knowledge!

Happy Reading.

Dr. Ashok Kumar MD, PhD, FICMCH, FICOG, FAMS
President, AOGD
Vice Chairperson, Elect, ICOG, an Academic Wing of FOGSI
National Corresponding Editor, Journal of Obstetrics & Gynaecology of India
Director Professor & Head
Department of Obstetrics & Gynecology,
Atal Bihari Vajpayee Institute of Medical Sciences &
Dr. Ram Manohar Lohia Hospital, New Delhi

Message from the Vice President

Vice President

Dear all,

Immense gratitude to esteemed seniors and all members of AOGD for having faith and trust in team ABVIMS and RML and bestowing upon me the responsibility of Vice President of AOGD. Our society is a large organization that provides abundant opportunities to meet, learn, teach, network, and give back to our community. I am proud of AOGD successes over last year especially in the field of professional development and outreach programs. In the year ahead we will continue those initiatives as well as add programs and events to be held in collaboration with other chapters in the Delhi NCR area. We as a team at RML though first-timers, are excited, eager, and energized to serve the society and are open to feedback from members and advice from seniors as to how we can serve you better. It is through our collective efforts that we can steer the organization toward greater success and better impact. Looking forward to a fruitful and wonderful year with support from all.

Dr. Indu Chawla Chugh

Vice President AOGD

Message from the Hon. Secretary

Hon. Secretary

Dear AOGD Members,

Warm greetings to all from AOGD secretariat at ABVIMS & Dr. RML hospital.

It is an honour and proud privilege to represent AOGD as an honorary secretary for the tenure 2024-25. I thank all AOGD members for entrusting us in this journey of taking AOGD to greater heights whilst maintaining the highest standards of professional and academic excellence.

At the core of our mission lies a vision that drives us forward every single day – a vision of comprehensive, compassionate, and accessible healthcare for women across Delhi. We believe that empowering women with knowledge about their health is essential for ensuring healthy outcomes. Through our educational initiatives and outreach programs, we aim to equip all our doctors with information and resources helping them become confident decision-makers. The theme of this year "Shared decision making – Enhancing women emancipation" will focus on empowering women as well as their healthcare providers, through various knowledge-building programs planned throughout the year.

We are happy to announce the dates for our annual conference, as 22nd, 23rd and 24th Nov 2024. The pre-conference workshops shall be conducted on 22nd Nov. We are looking for enthusiastic participation from all AOGDians. Our dedicated editorial team has been working hard and we present to you the first bulletin of the year focusing on "Maternal Fetal medicine".

I am thankful to our president Dr. Ashok Kumar, for entrusting me to perform the duties of the Secretary for this august organization. With guidance from our president, vice president, and seniors and hard work from the entire team, I am sure you will see a year full of academic activities and educational events. I seek blessing from all our teachers and well-wishers and embark on this journey with prayers from the almighty.

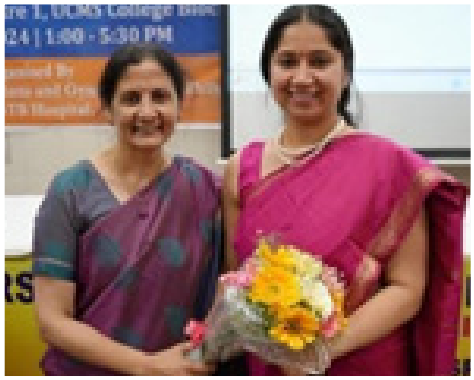
गुरुर्ब्रह्मा गुरुर्विष्णुर् गुरुर्देवो महेश्वरः।
गुरुः साक्षात् परब्रह्म तस्मै श्रीगुरवे नमः॥

Left to Right: *Dr. Vandana Agarwal, Dr. Neha Pruthi Tandon, Dr. Kamna Dutta and Dr. Geetanjali Nabiyal*

27th March 2024

Handing Over Ceremony From GTB & UCMS Hospital to ABVIMS & Dr. RML Hospital

Dr. Amita Suneja Handing Over Presidentship to Dr. Ashok Kumar



12th April 2024

AOGD Celeberation @ Dr. RML Hospital

ABVIMS & Dr. RML Hospital celebrated its taking over AOGD, first time in the history. Felicitation ceremony was followed by vision 2024-25 presentation by president AOGD Dr. Ashok Kumar following which two interesting talks were presented by Dr. Hemant Deshpande and Dr. JB Sharma respectively.

10th April 2024: Community Health and Public Awareness Subcommittee in association with Safe Motherhood Committee FOGSI and Directorate of Family Welfare-Workshop on basic antenatal care for ASHA workers

10th April 2024: Safe Motherhood Subcommittee - Webinar on "Placenta accreta spectrum disorder"

18th April 2024: Community Health and Public Awareness Subcommittee in association with Public Awareness Committee FOGSI - Health camp organized at Sri Aurobindo College.

19th, 20th and 21st April 2024

FOGSI Managing Committee Meeting at Kolkata

- AICOG 2026 preparation was presented
- Dr. Ashok Kumar, president AOGD and Dr. Neerja Bhatla, vice president FOGSI participated in the publication cell committee.
- Dr. Ashok Kumar participated in the ICOG governing council meeting and Journal of Obstetrics and Gynaecology of India (JOGI) meeting

20th and 21st April 2024: Urogynaecology Subcommittee - 1st Annual conference of Female Pelvic Pain Association

22nd April 2024: Safe motherhood subcommittee - CME cum Workshop on "Postpartum Haemorrhage Maternal Saviour: Fighting Postpartum Haemorrhage" at DDU Hospital

CME Cum Workshop on Postpartum Hemorrhage
Maternal Saviour: Fighting Postpartum Hemorrhage"
Organized by DDU Hospital
Under the aegis of the Safe Motherhood Committee, AOGD
Monday | 22nd April, 2024 | 1:30 - 4:30 PM
Venue: Seminar Hall, 3rd floor, Emergency & Trauma Block, DDU Hospital Harinagar

Dr BL Chaudhary, MD, DDUH — Dr Ashok Kumar, President AOGD — Dr Indu Chawla, Vice President AOGD — Dr Kanna Datta, Secretary AOGD
Organising Chairperson — Convener
Dr Poonam Laul, HOD, Dept of OBG, DDUH — Dr Shashi L Kalra Maheshwari, Chairperson, Safe Motherhood Committee, AOGD
Master of Ceremony: Dr Alokhya

Time	Topic	Speaker
1:30 - 2:00 PM	Lunch	
2:00 - 2:10 PM	Welcome Address & Felicitation of Dignitaries	
Session 1		
Chairpersons: Dr M Mani, Dr Vivek Bajpai, Dr Achala Batra		
2:10 - 2:20 PM	Overview of PPH & Medical Management	Dr Urvashi Miglani
2:20 - 2:35 PM	Surgical Management of PPH	Dr Shashi L Kalra Maheshwari
2:35 - 2:45 PM	Bench to Bedside -Where Did We Miss?	Dr Poonam Laul
Session 2		
2:45 - 4:30 PM	Demonstration on Work Stations	
	Station 1: Demonstration of PPH tool kit	Dr Sunita Seth
	Station 2: Quantitative Estimation of Blood loss & Demonstration of Blood & Components	Dr Niharika Dhiman
	Station 3: Brace Sutures	Dr Sonu, Dr Shashi L Kalra Maheshwari
	Station 4: Uterine Balloon - Condom & Chhattisgarh	Dr Usha Yadav
	Station 5: Bakri Balloon, Bhavi Balloon	Dr Kanna Datta
	Station 6: NASG	Dr Sushma Sinha
	Station 7: Demonstration of IIAL on model	Dr Shashi L Kalra Maheshwari
	Demonstration of IIAL in Cadaver	Dr Urvashi Miglani, Dr Harvinder Kaur
4:30 PM	Vote of Thanks	Dr Poonam Laul

23rd April 2024: Adolescent Subcommittee - Webinar on "Adolescent Mind: A Digital Maze, Decoding with the Experts"

WEBINAR ON
ADOLESCENT MIND: A DIGITAL MAZE -
Decoding with the Experts
Organized by: AOGD Adolescent Subcommittee
Tuesday | 23rd April, 2024 | 2:45 - 4:30 PM

Guests of Honour
Dr. Sharda Jain, Sec Gen DGF, Patron AOGD — Dr. Ashok Kumar, President AOGD 24-25
Organising Chairperson: Dr. Jyoti Bhaskar, Chairperson Adolescent Subcommittee of AOGD
Organising Secretary: Dr. Kiran Chhabra, Sr Consultant Obgyn, Vice President DGF-NW — Dr. Taruna Dua, Vice President DGF SW

Academic Session
Session 1 - 3:00 - 3:30 PM
Speaker
Dr. Manoj Sharma, Prof. Clinical Psychology NIMHANS Bengaluru
Digital Detox: Signs and Solutions to Digital Well being
Chairpersons
Dr. Ashis Batra — Dr. Meenakshi Ahuja — Dr. Taruna Dua — Dr. Dipti Nath
Session 2 - 3:45 - 4:15 PM
Speaker
Dr. Preeti Galgali, Adolescent Health Specialist & Paediatrician
HEEADSSS - An Adventurous walk through Adolescent Minds
Chairpersons
Dr. Anita Saraja — Dr Indu Chawla — Dr. Kiran Chhabra — Dr Mona Gupta
4:15 - 4:30 PM - Audience Interaction
Master of Ceremony
Dr. Neha Kapoor — Dr. Soyuita Khanjo

25th April 2024:

Oncology Subcommittee in collaboration with MEC of FOGSI & Assosciation of Gynae Oncologists of India (AGOI) on Webinar 5 "Management of Cervical Cancer" Gearing Up for Cervical Cancer Elimination Series.

26th April 2024: Monthly clinical meeting organized by LHMC

1. Hematuria - An Unusual Presentation of Placenta Accreta Spectrum
   Dr. Reena Yadav,
   Dr. Kanika Chopra
2. A rare complication of Cesarean Scar
   Dr. Kiran Aggarwal,
   Dr. Mansi Kumar
3. Enlarged Multicystic Ovaries in an Infertile Woman - Thinking Beyond Controlled Ovarian Stimulation
   Dr. Aishwarya Kapoor

28th April 2024: Postgraduate Academic Fiesta at ABVIMS & Dr. RML Hospital

29th April 2024: Cervical and Breast Cancer Prevention and Awareness Subcommittee - Webinar on "Cancer Prevention in Young Women"

30th April 2024: Endoscopy Subcommittee - Webinar on "Hysteroscopy - Revisiting the Basics"

Forthcoming Events

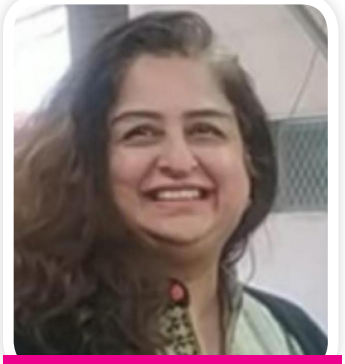
- 3rd May 2024 - A webinar on Demystifying endometriosis Part 1 will be organised by ABVIMS & Dr. RML Hospital
- 12th May 2024 CME - "Anaemia in pregnancy-Optimising mother and babies" at ABVIMS & Dr. RML Hospital
- 18th May 2024 CME - "Basic endoscopy" at ABVIMS & Dr. RML Hospital
- 25th May 2024 - The Medicolegal Subcommittee's first certificate course session at BLK Hospital
- 28th May 2024 - CME on Menstrual hygiene day by ABVIMS & Dr. RML Hospital
- 29th May 2024 - "Hands on workshop on PPH" at ABVIMS & Dr. RML Hospital
- 31st May 2024 - Monthly clinical meeting by BLK Hospital

Awards and Prizes

The following AOGDians were awarded in Practical Obstetrics Committee & Young Talent Promotion Committee FOGSI 2024, E-MOM Series - 3

- Dr. Shashi Lata Kabra DDU Hospital, Delhi - First prize - PPH Drill
- Dr. K Aparna Sharma AIIMS, Delhi - First Prize - Shoulder Dystocia Drill
- Dr. Mamta Dagar SGRH, Delhi - Third Prize - Maternal Collapse Drill

From the Editors Desk



Chief Editor

With great enthusiasm, we launch this AOGD bulletin 2024-25 from the new desk, which has come for the first time to ABVIMS & Dr. RML Hospital. AOGD is one of the most vibrant societies of FOGSI comprising a huge number of senior and highly experienced patrons and members guiding and leading the way for an enthusiastic young brigade of gynaecologists. AOGD Bulletin is a platform dedicated to advancing the knowledge and empowering obstetricians and gynaecologists of Delhi. We recognize the critical role Ob-Gyn plays in shaping women's health across every life stage, and we aim to be a comprehensive resource for evidence-based practices, insightful clinical experiences, and cutting-edge research. Stay tuned for groundbreaking research, insightful case reviews, and stimulating discussions on the ever-evolving landscape of OB-GYN.

We have a vibrant editorial team that induces an infusion of youthful energy in the journal. We are incorporating certain new ideas like interesting case reports which are now invited for publication, an academic news section, ISSN indexation, and many more. In our first issue we delve into the captivating world of Maternal Fetal Medicine. It focuses on the critical role that fetal medicine plays in ensuring the good health and well-being of expectant mothers and their babies during high-risk pregnancies. We will explore the latest advancements in maternal-fetal medicine beginning from cutting-edge diagnostic tools to innovative new interventions along with adding on to the updates in the existing literature. Join us as we unravel the complexities of maternal-fetal medicine in this first issue.

We are confident that this journal will become an indispensable resource for all those dedicated to providing exceptional care to women. We envision this journal as a vibrant hub for knowledge exchange and collaboration.

Carpe Diem !

Dr. (Prof) Renuka Malik

Editor

Professor and Senior Consultant, ABVIMS & RML Hospital

Editorial Team: (Left To Right) Dr. Kanika, Dr. Preeti, Dr. Renuka, Dr. Kavita.
(Second Row Left To Right) Dr. Seema, Dr. Niharika

Thought for the month: There is only one way to avoid criticism: do nothing, say nothing, and be nothing – Aristotle

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Screening in First Trimester – Inverting the Pyramid of Care

Dr. K. Aparna Sharma[1], Dr. Akanksha Gupta[2]

Professor[1], Senior Resident[2]

Department of Obstetrics and Gynaecology, AIIMS, New Delhi

INTRODUCTION

Pregnancy is a unique experience of 9 months in the life of a woman when she comes in contact with the health care providers and providing a positive pregnancy experience is now considered paramount both for the health care providers and the policy makers. In 2016 WHO increased the frequency of ANC visits from 4 to 8 with the idea of increased opportunities to detect and manage potential complications of pregnancy that arise and reduced likelihood of stillbirths with the first contact of pregnant women at 12 weeks.

However, studies in recent years have shown that the majority of pregnancy complications arising later on in pregnancy are predictable with a multitude of tests. Hence, shifting the focus toward the prediction rather than of such complications. Early prediction provides us with an opportunity to classify women at risk of dreaded complications like Preeclampsia, Fetal growth restriction, and Fetal congenital anomalies. By classifying women at a high risk for complications in later gestation and those at very low risk, a prenatal care plan can be developed that is tailored to individual patients, thus, inverting the pyramid of prenatal care (Fig. 1 A & B).

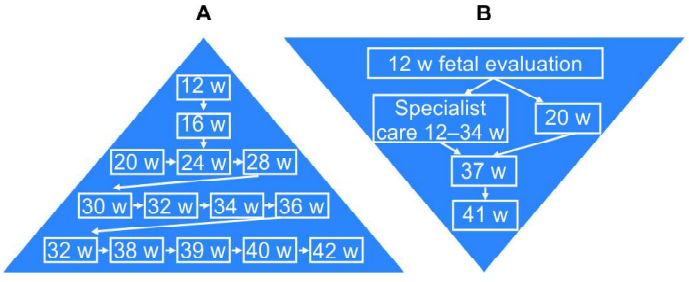


Fig. 1: (A) Routine ANC pathway; **(B)** Inverted pathway of ANC care[1]

Benefits of an Inverted Pyramid of Antenatal Care

A cost-effective pathway of ANC care can be achieved by shifting from primary to primordial prevention and effective utilization of resources especially in a resource-limited country like India where the majority of resources are utilized for managing pregnancy complications.

Also, resource allocation for effective preventive strategies and timely institution of treatment will ensure positive pregnancy outcomes and reduce maternal and neonatal morbidity and mortality.

Components of First Trimester Screening

1. First-trimester aneuploidy screening
2. Screening for Anomalies
3. Preeclampsia screening
4. Screening for FGR
5. Screening for preterm labor
6. Screening for Diabetes

ANEUPLOIDY SCREENING

Who Should be Screened?

The recommendation:

The need for screening for aneuploidies cannot be emphasized more since it is a preventable cause of congenital abnormalities in fetuses. The overall prevalence of aneuploidies is 4 per 1000 births.

Aneuploidy accounts for:

1. >50 percent of first-trimester abortions
2. 20 percent of second-trimester losses
3. 6 to 8 percent of stillbirths and early childhood deaths[2]

As around 90% of pregnancies occur in women <35 years of age and 80% of Down syndrome infants are born to women <35 age and if all women >35 accepted amniocentesis, only 20% of DS cases were identified. Hence, to decrease the number of invasive procedures, and to alleviate the parental anxiety related to aneuploidies and recurrent abortions universal screening of all pregnant women is recommended to screen for high-risk women[3].

ACOG also recommends prenatal genetic screening and diagnostic testing options should be discussed and offered to all pregnant women regardless of maternal age or any other risk factors and all patients have the right to accept or decline testing after counseling.

Table 1: Points of Pretest and Post-Test Counseling

Pre-test Counseling	*Post-Test Counseling*
Points in Counseling: • Inform regarding chromosomal disorders • Inform regarding the specific risks of carrying a fetus with a chromosomal abnormality • Review relevant personal and family history • Discuss risks, limitations, and benefits of available tests	*Test Negative: Discuss* • Concept of residual risk (the chance that an abnormality may still be present even if the test result is screen negative) • Consider the detection rate of each test • Consider conditions targeted in screening *Test Positive:* • Provide information on the likelihood of fetal affection (PPV) • Options for additional testing

What are the Screening Approaches Available?

Table 2: First Trimester Aneuploidy Screening Approaches

Screening approach	*POG (Weeks)*	*Markers*	*Detection rate for trisomy 21 (%)*
Nuchal translucency scan	11-13 6/7	NT	70
Dual marker	11-13 6/7 (free beta hcg) 10-13 6/7 (total beta hcg)	PAPP – A and Beta HCG	70
Combined test	11-13 6/7 (free beta hcg) 10-13 6/7 (total beta hcg)	1. Maternal age 2. PAPP-A and Beta HCG 3. NT	82-87
NIPS	9-10 weeks to term	Cell-free fetal DNA	99%

Note – false positive rate for all approaches – 5% except NIPT – 0.07%

SCREENING FOR ANOMALIES

NT scan is now regarded as a mini anomaly scan and provides much more information than just aneuploidy screening. In a 2017 systematic review of 30 studies from 1991 to 2014, the sensitivity of first-trimester ultrasound screening for detection of fetal anomalies in low-risk or unselected populations was 32 percent (95% CI 22-43 percent) and, in high-risk populations, 61 percent (95% CI 38-82 percent). When only major anomalies were considered, sensitivity in low-risk or unselected populations was 46 percent. An anomaly of any type was present in 1.8 in 100 fetuses in low-risk pregnancies and 6.6 in 100 fetuses in high-risk pregnancies; a major anomaly was present in 1 in 100 fetuses in low-risk pregnancies. No information was available on specific anomalies. Most patients will need a second-trimester survey to provide a more reliable assessment of fetal anatomy[4].

SCREENING FOR PREECLAMPSIA

Screening by Maternal History

Most of the professional bodies recommend that at the booking visit, a detailed history should be taken and guidelines for the same (Table 1). Estimated DR of PE requiring delivery before 34, 37, and 42 weeks of gestation in screening by maternal factors are about 51, 43, and 40% respectively at an FPR of 10% (17). Despite such low detection rates most of the professional bodies including ACOG recommend taking a detailed medical history only to assess a patient's risks for developing preeclampsia[5]. (Table 3)

Table 3: Risk factors to be considered while taking history in the first trimester

ACOG 2018 (5)	
High Risk	*Moderate Risk*
• Previous pregnancy with PE	• Nulliparity
• Chronic Hypertension	• Age more than 35 y
• Systemic lupus erythematosus	• Interpregnancy interval >10 y
• Type 1 or type 2 diabetes mellitus	• BMI >30 kg/m^2
• Renal disease	• Family history of PE (mother or sister)
• Multifetal gestation	• History of SGA or adverse outcome
• Antiphospholipid syndrome	• Socio-demographic characteristics (African American race or low socioeconomic status)

Screening by Maternal Biophysical Markers

Blood Pressure

Women who subsequently develop PE have higher systolic blood pressure and MAP before the onset of clinical disease. MAP is calculated by adding one-third of the pulse pressure to the diastolic pressure. MAP should be measured by validated automated devices with women in sitting positions with their backs supported and legs uncrossed. Arms should be well supported at the level of their heart, and an appropriate-sized adult cuff (small <22 cm, normal 22–32 cm, or large 33–42 cm) should be used. After resting for 5 minutes, BP is measured in both arms simultaneously. Two sets of recordings are made at 1-minute intervals. The four sets of SBP and DBP measurements are needed for input into the risk calculator. If MAP is taken in the first trimester along with maternal characteristics the detection rate of preeclampsia goes up to 74% for early preeclampsia and 49% for late preeclampsia with a false positive rate of 10%. If we measure MAP in both the first and second trimesters we have a detection rate of 84% for early preeclampsia and 53% for late preeclampsia with a false positive rate of 10%[6].

Uterine Artery Dopplers

The spiral arteries undergo a transformation to low resistance vessels by trophoblastic invasion and increase blood flow in the placental bed in pregnancy[7]. If this mechanism fails, it leads to defective placentation. The uterine artery PI MoM is significantly increased at 11–13 weeks gestation in women who subsequently develop PE. The addition of uterine artery PI to maternal factors improves the DR from 51 to 75% and 43 to 55% at an FPR of 10% for PE requiring delivery before 34 and 37 weeks' gestation[6]. A sagittal section of the uterus using a transabdominal scan should be obtained then the cervical canal and internal cervical os need to be identified using Colour flow mapping each uterine artery along the side of the cervix and uterus at the level of the internal os is identified. Pulsed wave Doppler is then used with the sampling gate set at 2 mm to cover the whole vessel and care should be taken to ensure that the angle of insonation is less than 30. When three similar consecutive waveforms are obtained the PI is measured and the mean PI of the left and right arteries is calculated[8]. It is important to ensure that the peak systolic velocity is greater than 60 cm/s (Fig. 2)

Screening by Maternal Biochemical and Biophysical Markers

Effective screening for PE can also be achieved by a combination of maternal factors, and biochemical and biophysical markers. If MoM values of serum PAPP-A and PlGF, MAP, and uterine artery PI in pregnancies with PE, are added to the maternal characteristics. all four markers together increase the risk assessment of preeclampsia. Estimated DR of PE requiring delivery before 34, 37, and 42 weeks gestation in screening by maternal factors with biochemical and biophysical markers are 96, 77, and 54%, respectively, at an FPR of 10%[6].

Algorithmic Approach: Multimodality

All pregnant women should be screened for preterm PE during early pregnancy by the first-trimester combined test with maternal risk factors and biomarkers as a one-step procedure. The risk calculator is available free of charge at https://fetalmedicine.org/research/assess/preeclampsia[9]. FIGO encourages all countries and its member associations to adopt and promote strategies to ensure this. The best-combined test is one that includes maternal risk factors, measurements of mean arterial pressure (MAP), serum placental growth factor (PlGF), and uterine artery pulsatility index (UtPI). A woman is considered high risk when the

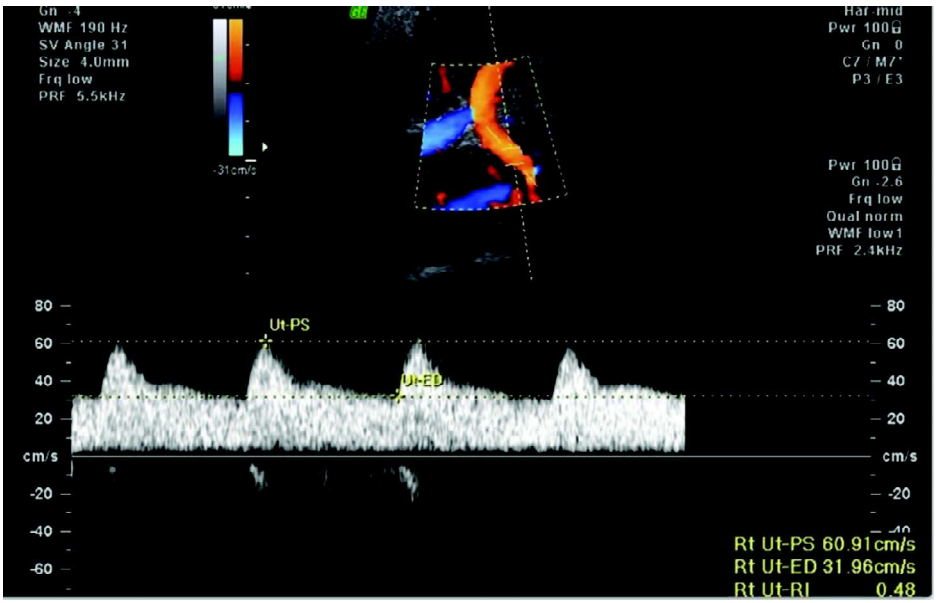


Fig. 2: Measurement of uterine artery PI

risk is 1 in 100 based on the first-trimester combined test with maternal risk factors, MAP, PlGF, and Uterine artery PI.

SCREENING FOR FETAL GROWTH RESTRICTION SCREENING FOR FGR

Fetal growth restriction (FGR) is a major cause of stillbirth and poor neurodevelopmental outcomes. Early prediction is important to establish surveillance methods for detection and improve neonatal outcomes. The prediction is similar to PE as one-third of early FGR is due to PE. However, a combination of several maternal characteristics, biophysical parameters (BP and Uterine Artery Doppler), and angiogenic factor levels (PlGF and sFlt-1) achieved DRs for early and late FGR of 86% and 66%, respectively, with an FPR of 10%.

It was seen that the sFlt-1: PlGF ratio improved the DRs by 27% for early FGR and 24% for late-onset forms, emphasizing the potential role of these biomarkers for predicting growth restriction. First-trimester screening performance is poorer for late FGR, but PlGF and sFlt-1 increased the DRs to an acceptable level. These models remain useful in normotensive cases[10].

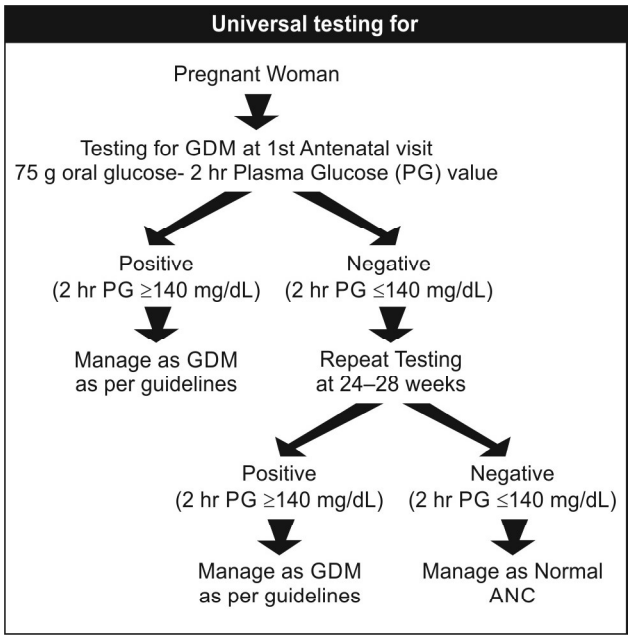
FASTER trial evaluating the role of uterine artery PI and PAPP-A in a large cohort of women established the role of both in predicting Fetal growth restriction. Although, the association was poor, paved the way for further studies. Another meta-analysis of 32 studies also established a poor association of PAPP-A and uterine artery PI in 1st trimester for FGR prediction. However, it was found that the combination of maternal history, abnormal uterine artery Doppler, and low PAPP-A level at 11–14 weeks were better predictors for small gestational age fetuses than both markers alone[11].

SCREENING FOR PRETERM LABOUR

Women with a history of preterm birth are at high risk of subsequent preterm births hence all societies ACOG, SMFM, and RCOG recommend screening with serial cervical length from 16 to 24 weeks gestation. Unfortunately, evidence regarding the utility, feasibility, and cost-effectiveness of universal transvaginal cervical length screening in low-risk populations is conflicting. Although, many institutions practice universal cervical length screening protocols, evidence regarding the effectiveness of this practice is in evolution[12].

SCREENING FOR GDM

GDM has emerged as a global public health problem. In India alone, GDM complicates nearly 4 million pregnancies annually, representing a large subset of the population at high risk for adverse perinatal morbidity and mortality if left inappropriately managed. Beyond perinatal implications, GDM marks the beginning of a vicious cycle in which Diabetes begets Diabetes, leaving a legacy for both the affected mother and her offspring to face impending long-term consequences like Type 2 DM and other Non-Communicable Diseases(NCD).



Ministry of Health Government of India mandates screening all pregnant women for Gestational Diabetes Mellitus (GDM) as part of a routine antenatal package. Hence, the current recommendation is, that all pregnant women should be screened for Gestational Diabetes Mellitus, even if they have no symptoms[13]. The present concept is to screen for GDM in the early weeks of pregnancy, if negative to be repeated in the subsequent weeks of pregnancy as GDM manifests in all the trimesters of pregnancy[14].

CONCLUSION

The new challenge for improvement of pregnancy outcomes will be met by inverting the pyramid of perinatal care by shifting series of routine visits to individualized patient and disease specific approach.

KEY POINTS

1. The inverted pyramid of prenatal care and monitoring is established for the purpose of prediction and prevention, early detection and treatment of health disorders of both mother and fetus.
2. Maximum fetal chromosomal and structural anomalies can be diagnosed in the first trimester of pregnancy.
3. The risk of some pregnancy complications that become evident in later pregnancy can be predicted in first trimester so the incidence of these complications can be reduced by instituting treatment early in pregnancy.

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Monthly Clinical Meetings AOGD Calendar 2024-25

Date	Hospital
26th April, 2024	LHMC & Smt. Sucheta Kriplani Hospital
31st May, 2024	B L Kapoor Hospital
28th June, 2024	Apollo Hospital
26th July, 2024	Army Hospital (Research & Referral)
30th August, 2024	AIIMS Delhi
27th September, 2024	ESI, Basaidarapur Delhi
25th October, 2024	DDU Hospital
29th November, 2024	MAMC & LNJP Hospital
27th December, 2024	Sir Gangaram Hospital
31st January, 2025	VMMC & Safdarjung Hospital
28th February, 2025	UCMS & GTB Hospital
28th March, 2025	RML Hospital
25th April, 2025	LHMC & Smt Sucheta Kriplani Hospital

Recent Advances in Genetic Testing

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Senior Consultant

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INTRODUCTION

Congenital malformations are common accounting for 3-4% children at birth. Incidence of chromosomal abnormalities at birth is 0.6%. Incidence of single gene disorders at birth is 1-2%. Majority of genetic disorders lead to mental or physical handicap. Diagnosis and management of such disorders is difficult and challenging and hence prevention through prenatal diagnosis is the only way forward. There has been a paradigm shift in genetic testing in last two decades. Concept of genomic testing has revolutionised the genetic testing. Traditional genetic tests look at one or a few disorders at a time. Genomic tests can look at hundreds or thousands of genes/ disorders in one single test, yielding much more information in one single test. A next generation physician needs to understand the basics of medical genetics and recent technical advances so as to improve the standard of patient care. This is important for practicing obstetricians as well who have to do genetic testing at various points in a woman's life:

INDICATIONS FOR GENETIC TESTING

1. Preconception carrier testing for genetic disorders
2. Prenatal screening and diagnosis of genetic disorders
3. Recurrent abortions
4. Primary/ Secondary amenorrhoea
5. Male infertility
6. Genetic testing following abortion, fetal demise
7. Genetic testing prior to implantation
8. Genetic testing for hereditary breast and ovarian cancer

Broad categories of genetic disorders include single gene disorders, CNV (Copy number variations), and chromosomal abnormalities. So, the genetic testing is for two basic types. (Table 1)

1. Cytogenetic testing for chromosomal abnormalities
2. Molecular testing for single gene disorders

Table 1: Types of genetic testing

Cytogenetic testing	*Molecular testing*
1. Karyotype	1. PCR, RFLP, ARMS
2. Fluorescent in situ hybridization	2. Sanger sequencing 3. Tests for Triple repeat disorders
3. Chromosomal microarray	4. Next Generation Sequencing

Chromosomal Disorders can be

- Numerical (aneuploidy) changes in the number of chromosomes
- Structural changes of chromosomes

Down syndrome, Trisomy 18, Trisomy 13 are numerical abnormalities due to the changes in chromosome number

Balanced translocations, inversions and insertions are due to structural changes in the chromosomes.

Smaller chromosomal areas that are lost or gained are known as copy number variations (CNV), and they are linked to a variety of human disorders e.g. Digeorge syndrome

Single gene disorders are caused by sequence variation in the genes e.g. Thalassemia, Duchenne muscular dystrophy

Cytogenetic testing includes Karyotype, FISH and microarray. Cell free fetal DNA is also for detecting chromosomal aneuploidies from maternal plasma during pregnancy.

Salient features of cytogenetic testing are mentioned in Table 2.

Table 2: Cytogenetic testing

Karyotype	*FISH- Fluorescent in situ hybridization*	*Chromosomal microarray*
Resolution: 5-10 Mb	Resolution: average 80kb -1 Mb for constitutional aberrations	Resolution: down to 50kb (or less)
Needs expert eyes for interpretation	Locus specific- we need to know the targeted region.	100% sensitivity and specificity for 400kb CNVs
Time consuming (2-3 weeks for results)	FISH is considered a validation NOT a screening test	Results in 3 days
Cannot detect LOH, UPD	Fluorescence microscope required	User friendly software for data interpretation
LOH- Loss of heterozygosity, uniparental disomy		SNP probes allow detection of LOH, UPD, parent of origin and consanguinity

KARYOTYPE

- Karyotyping is for detecting chromosomal abnormalities and is considered as gold standard
- The complete set of chromosomes in an organism is called its karyotype.

Indications of Karyotype include

- Positive dual screen/ quadruple screen
- Positive NIPT for aneuploidy
- Newborn with ambiguous genitalia
- A girl with short stature
- Recurrent abortions
- Primary amenorrhea
- Azoospermia/oligozoospermia- when total sperm count is <5-10 million
- POC- products of conception

Clinical Utility

Commonest indication to do the karyotype for obstetrician is a couple with three or more spontaneous abortions. This is done to exclude balanced translocation carrier. (Fig. 1)

About 5% of couples with recurrent miscarriages are balanced translocation carriers. Although balanced translocation carriers are themselves healthy, they may give rise to unbalanced gametes at gametogenesis and the partial monosomy/ trisomy of the parts involved which results in recurrent miscarriages or a child with mental retardation. Reproductive options for such couples are –

1. Spontaneous conception followed by amniocentesis at 16 weeks for karyotype/ chromosomal microarray
2. IVF with PGT-SR (Preimplantation genetic testing-structural rearrangements)
3. Donor oocyte/ donor sperm
4. Adoption

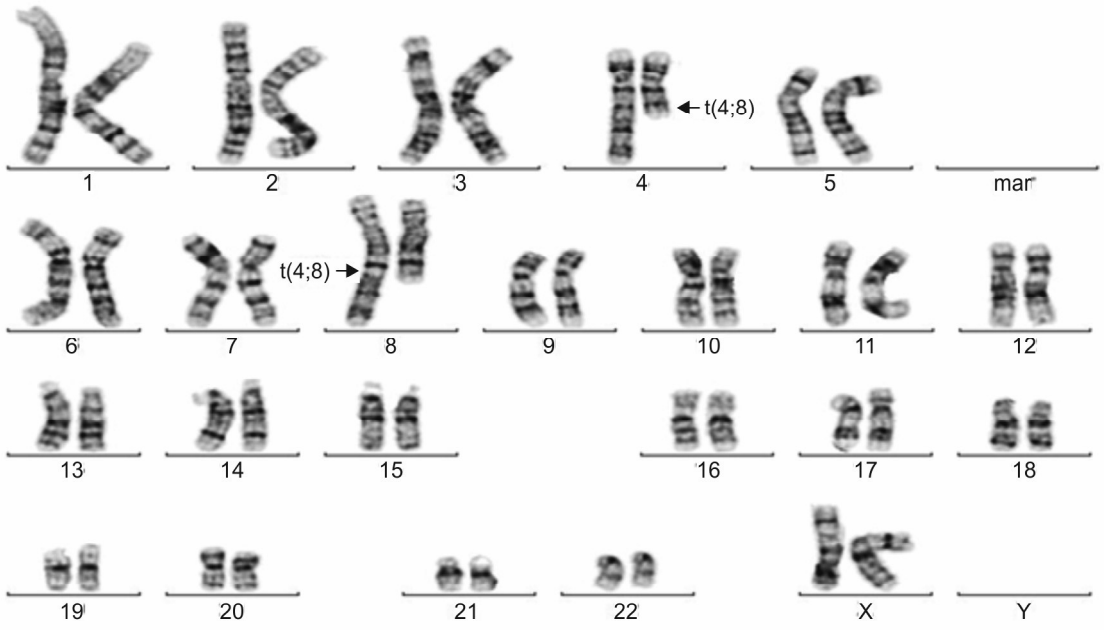

Fig. 1: Karyotype

Couples with good fertility should be encouraged for spontaneous conception and followed by amniocentesis. IVF-PGT-SR should be offered to couples with subfertility.

FLUORESCENCE IN SITU HYBRIDIZATION (FISH)

The most commonly used test for identifying chromosomal abnormalities is karyotyping.

Karyotype, on the other hand, cannot identify cytogenetic anomalies smaller than 5 Mb. FISH is a targeted technique that can identify numerical and structural abnormalities of cytogenetic aberrations smaller than 5 Mb

Indications for FISH

1. Prenatal diagnosis of 5 common aneuploidies after positive soft marker on screening test
2. Newborn with ambiguous genitalia
3. Suspected genetic syndrome- Digeorge, Prader willi, Angelmann syndrome, Turner
4. History of suspected cryptic balanced translocation in couple
5. POC- products of conception

Conventional fish does not allow a comprehensive evaluation of the whole genome. Fish provides high resolution analysis of only targeted locations and is indicated if diagnosis is already known

Clinical Utility

Commonest indication of FISH is rapid aneuploidy diagnosis on amniotic fluid to exclude common aneuploidies on amniotic fluid or chorionic villi sample.

CHROMOSOMAL MICROARRAY ANALYSIS (CMA)

This is a cytogenomic tests and now commonly used to detect numerical chromosomal abnormalities including CNV's.

Compared to routine karyotyping microarray has higher resolution. ACMG guidelines suggest CMA as the first line investigation of children with intellectual disability, multiple malformations and autism as per ACMG guidelines and thus replacing karyotyping for these indications. A far higher diagnostic yield is provided by CMA. (15%–20%) compared to karyotype.

In the case of foetuses with abnormal ultrasound results, CMA is superior than karyotyping. This was demonstrated first in a landmark study funded by National Institute of Child Health and Human Development (NICHD). The study showed that clinically significant copy number variants (CNVs) were identified in 6% (45/755) of foetuses with

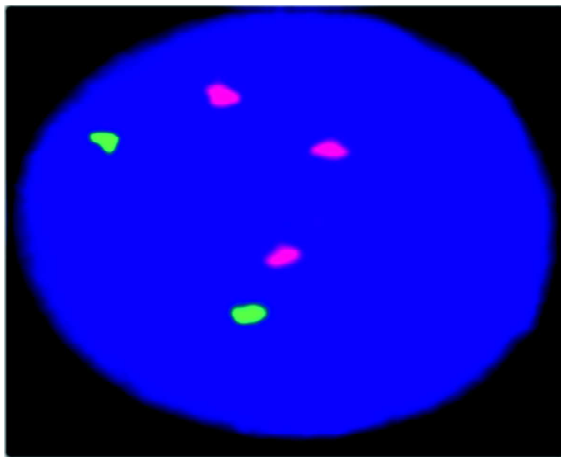

Fig. 2: FISH on AF: interphase cell showing two green signals for chromosome 13 and three orange signals for chromosome 21, indicating Presence of Trisomy 21 (Down's Syndrome)

anomalies.[1] American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal-Fetal Medicine (SMFM) guidelines recommend that CMA should be done in all cases with ultrasound detected fetal anomalies.[2,3] In cases of soft markers and fetuses with positive biochemical screen but no ultrasound anomalies, this can be offered in view of increased detection rate (1.7%) compared to karyotype.[1]

CMA- BASIC CONCEPTS

A DNA microarray is a huge assembly of bits of DNA placed onto a solid surface, such as glass. It resembles a computer chip. These DNA fragments are DNA probe and size of DNA probe is - 25 to 80 base pairs. Human genome contains over 3 billion base pairs, so a DNA microarray would require multimillion probe in order to comprehensively cover the entire genome. CMA probes are intelligently designed to cover coding or noncoding functional genes and are usually enriched for clinically significant regions. They can identify single nucleotide polymorphisms (SNPs), CNVs, or both.

Types of CMA

There are two techniques used for identifying chromosomal imbalance using CMA:

- Comparative genomic hybridization (CGH) and
- SNP- Single nucleotide Polymorphism

Compared to aCGH,SNPs provide more even genome coverage and better detection of CNVs and can detect triploidy, UPD and Mosaicism

Commercially available platforms are designed as Hybrid arrays and contain oligonucleotide probes for detecting both CNVs and SNPs.

Interpretation

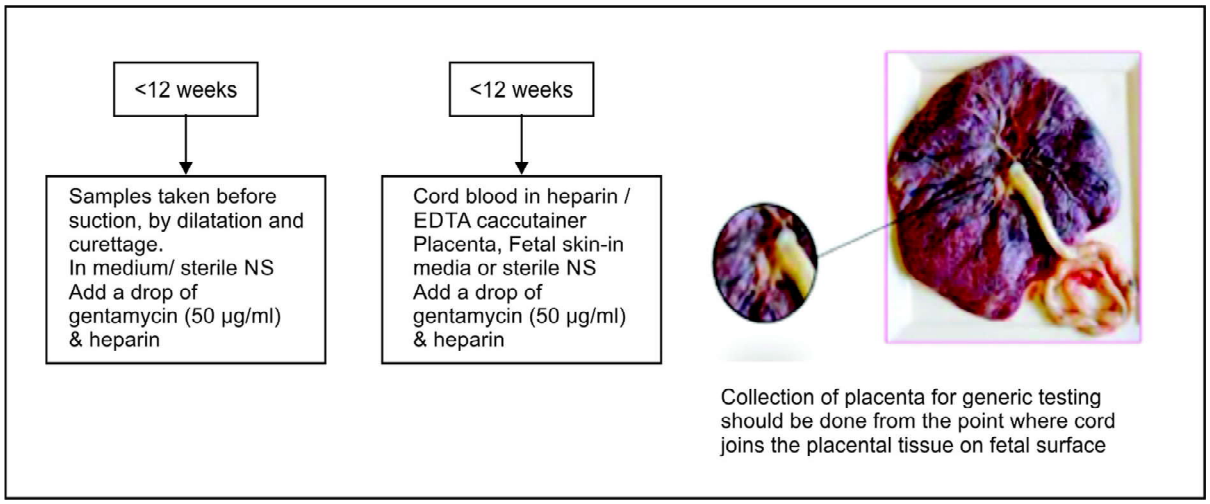

Fig. 3: How to collect POC sample

The databases used for CNV interpretation are Decipher, UCSC genome browser, Clinvar etc.

The CNVs are classified (based on American College of Medical Genetics and Genomics (ACMG) criteria)

- Pathogenic,
- Benign or
- Variant of uncertain significance (VOUS)

  A variant has been detected, but it is difficult to classify it as either pathogenic (disease causing) or benign (non-disease causing) based on current available scientific evidence
- To ascertain the significance of the variant Parental testing may be required.

A clinician must know the design and resolution of the testing platform and the genomic regions covered before ordering CMA. Most of the commercial platforms available have probes for known microdeletion/ duplication syndromes along with genome wide probes for other clinically significant CNVs. Microarray can be low resolution or high resolution depending upon the number of probes used. A typical 750 K microarray is sufficient for testing of a fetus with antenatal detected anomalies on ultrasound

Both pretest counselling (for the diagnostic sensitivity - detection rate 5-10% higher compared to routine Karyotye and limitations) and post-test genetic counselling are essential.

CMA has certain limitations:

- Unable to detect monogenic disorders
- Unable to detect balanced translocations
- Unable to detect mosaicism <10-15%
- VOUS- variation of uncertain significance
- Need of Parental studies

Clinical Utility

CMA is mainly needed for the analysis of products of conception in the routine obstetric practice after excluding maternal cell contamination. Fig. 3 shows how to collect a POC sample in case of abortion or fetal demise. A CMA with 750 K resolution is the ideal but a lower resolution CMA (315 K) can be done if there is a cost constraints. There are very few indications of POC FISH or karyotype.

NON-INVASIVE PRENATAL TESTING (NIPT)

The paradigm for prenatal testing has evolved with the introduction of non-invasive prenatal testing (NIPT), which provides a step in between invasive diagnostic testing and serum screening. The test is based on cell free DNA that comes from the mother and the foetus. The placenta or trophoblasts undergo apoptosis to produce "foetal" DNA, and hematopoitic cells are the source of maternal cell free DNA. Because both the placenta and the foetus are products of a single fertilised egg, they have identical genetic backgrounds, which serves as the foundation for NIPT using maternal plasma. Non-invasive prenatal testing, or NIPT, was first introduced in high-risk pregnancies in Asia through the commercial sector. Since then, it has extended throughout the world, covering not just common trisomies but also whole genome NIPT and some microdeletions.[4]

ACOG (2020) recommends that prenatal genetic screening and diagnostic testing should be offered to all pregnant women. Maternal Serum screening with or without nuchal translucency or cell-free DNA screening and diagnostic testing (chorionic villus sampling or amniocentesis) should be universal to all pregnant women regardless of maternal age.[5] ISUOG consensus statement recommends that all women should undergo a first-trimester ultrasound scan first according to ISUOG guidelines, and then should be offered three options- combined screen, NIPT or amniocentesis.[6]

The fetal fraction is the proportion of total cell-free DNA

that is fetal in origin. Accurate cell-free DNA screening requires a minimum fetal fraction, most commonly estimated at about 2–4%. A low fetal fraction can cause cell-free DNA test failure. ACMG recommends that all laboratories should notify the cause of test failures to referring obstetrician.

ISPD has recently published guidelines for NIPT in singleton pregnancy and suggest[7]

1. NIPT for the common autosomal aneuploidies to be offered in primary or contingent screening models.
2. NIPT for SCA (sex chromosome anomaly) should be offered alongwith common trisomy screening
3. NIPT for RATs (rare autosomal trisomies) is not recommended for the routine care of unselected populations.
4. NIPT for microdeletion syndromes is not recommended for the routine care of unselected populations.
5. Before ordering NIPT, one early first trimester scan for dating, fetal cardiac activity diagnosis of multiple pregnancy, NT and any anomaly should be done
6. Fetus with NT measurement ≥ 3.5 mm, and presence of any anomaly should be offered invasive testing for microarray

In twin pregnancy, Khalil et al suggest that NIPT is the most accurate available screening test than combined dual screen.[8]

Molecular tests for monogenic disorders include

1. Sanger sequencing
2. ARMS- PCR (amplification restricted mutation scanning), RFLP (restriction fragment length polymorphism)etc.
3. MLPA (Multiple ligation probe amplification)
4. Next generation sequencing (NGS)

NEXT-GENERATION SEQUENCING

NGS, also known as massively parallel sequencing or deep sequencing, is a high throughput sequencing technology which allows simultaneous sequencing of millions of DNA base pairs at a comparatively lower cost and higher speed. Exomes comprise only 1% of 6.2 billion base pairs in human DNA, which code for proteins.

NGS based analysis includes three major groups: Clinical exome sequencing (CES); Whole exome sequencing (WES); Whole-genome sequencing (WGS). (Table 3)

Exons are the protein-coding region of the genome, which make up 1% to 2% of the total genome, but more than 85% of all disease-causing mutations are reported in these regions. Exome sequencing cover only exons. Genome sequencing covers both introns and exons.

Table 3: Types of Next generation sequencing

Clinical Exome Sequencing	*Whole exome sequencing*	*Whole genome sequencing*
In clinical exome sequencing, only those genes are included which are known to be disease causative and the total number of genes in this would vary depending upon the laboratory, and generally, it can cover 5000- 7000 genes.	In whole exome sequencing, all exons are tested and testing would include around 20000 genes.	Whole genome sequencing involves testing of whole exons and introns and currently mainly used as a research tool.

Whole exome sequencing is mainly being used for suspected monogenic disorders. A trio analysis (child and parents) is the most ideal approach to genetic testing.

Clinical Utility

Carrier screening for genetic disorders is by expanded carrier screening by clinical exome or whole exome sequencing.

CMA is ordered first in a case with antenatal detected anomaly, a child with intellectual disability or congenital malformations/ autism. NGS should be the first choice if there is a family history or consanguinity or suspected single gene disorders. Fig. 4 shows a chart depicting genetic testing for various indications in the obstetric care.

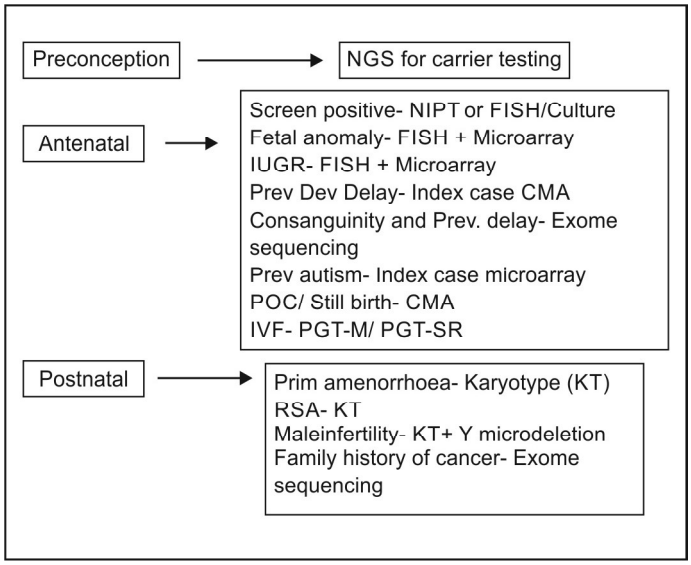

Fig. 4: Genetic/ Genomic testing in Obs & Gynae

CONCLUSIONS

- Genomic testing is rapidly becoming an integral part of clinical practice

- NIPT, Chromosomal microarray, exome sequencing and NGS techniques are powerful methods to diagnose the genetic etiology
- Hence, its important to be well versed with these tests so as to improve the evidence based health care standards

KEY POINTS

1. There are 2 major types of chromosomal disorders- numerical and structural
2. Genetic testing can be cytogenetic or molecular
3. Karyotype is gold standard for detecting chromosomal anomalies
4. CMA has higher resolution than karyotype
5. CMA is investigation of choice for analysis of products of conception

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AOGD Risk Management Support (ARMS) Group

One of the ways to ensure stress-free work environment and optimal patient care is mutual support among professional colleagues. An advisory group was set up last year so that they can be contacted if any of us is caught in a complex clinical dilemma/dealing with aggressive clients or is apprehensive about how to document or effectively troubleshoot a potential problem. The same group will continue to provide timely advice and is led by

Convener – Dr. Vijay Zutshi – 9818319110

Co-convener – Dr. Aruna Nigam – 9868656051

We invite suggestions from all members regarding functioning of this cell which will guide us forming the SOPs. Please mail to aogd.ucmsgtbh2023@gmail.com

Ultrasonographic Soft Markers

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INTRODUCTION

Soft markers are certain specific ultrasound findings identified in the mid-trimester that commonly do not represent a structural abnormality, may be transient, and are found in several normal fetuses. However, they are important as they are associated with an increased aneuploidy risk.

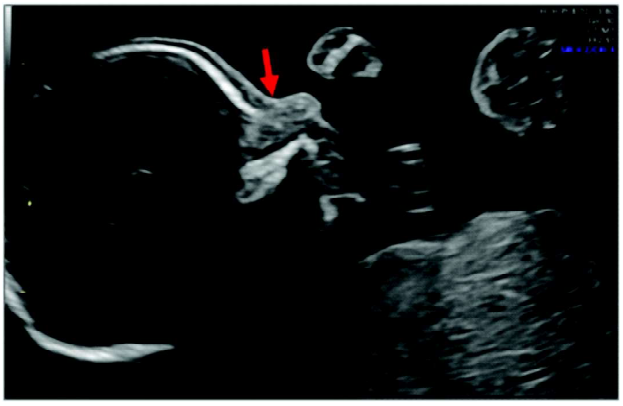

Fig. 1: 2 D gray scale ultrasound image mid sagittal view of fetal face showing absence of the second white line beneath the skin, suggestive of absent nasal bone.

Case courtesy: Dr. Priyanka Sharma, Director & Radiologist, Vital Point Diagnostics, Jaipur

Identifying a soft marker calls for a detailed obstetric ultrasound examination, to find if the soft marker is isolated, or has occurred in a cluster of other findings. The presence of a cluster of soft markers may point towards a specific chromosomal anomaly and is linked to an increased risk of congenital anomalies and preterm birth[1].

Most of the soft markers are associated with a minimal to moderate risk of aneuploidy. Therefore, for an isolated soft marker, current recommendations suggest an evaluation of risk factors for aneuploidy and non-invasive testing and if the cell-free DNA or quad screening is normal, diagnostic testing for aneuploidy is not indicated and the soft marker is to be considered as a normal variant or not clinically significant[2].

Soft markers are:- absent or hypoplastic nasal bone, thickened nuchal fold, choroid plexus cyst, echogenic intracardiac focus, echogenic bowel, short long bones, urinary tract dilation, and a single umbilical artery.

ABSENT OR HYPOPLASTIC NASAL BONE

As described by Sonek et al[3] the nasal bone is evaluated in the mid-sagittal view of the fetal face, and the correct image would show three echogenic lines, the first two lines proximal to the forehead appearing as an "equal to" sign (Fig. 1). It is defined as absent when the second echogenic white line beneath the skin is not seen, and hypoplastic based on nasal bone length (gestational age based centiles, <2.5th centile or < =2.5 mm), biparietal diameter to the nasal bone ratio (>=10 or >=11) or MoM (< =0.7 MoM)[2]. Although nasal bone is absent in 0.5-2.8 percent of normal fetuses[4], absent or hypoplastic nasal bone is considered a strong marker for aneuploidies, including trisomy 21, 18, 13 as well as Copy Number Variations, with an estimated prevalence of up to 73 percent in trisomy 21 at 11-14 weeks scan[5]. Therefore, when absent or hypoplastic nasal bone is seen, one should look for the presence of other soft markers and structural defects. There is a strong recommendation that the pregnant woman must be counselled and risk assessment and non-invasive screening tests or diagnostic tests for aneuploidy are to be done, according to patient preferences and clinical scenario. If the screening tests are negative and the only positive finding is absent or hypoplastic nasal bone, option of cfDNA or diagnostic testing or no further aneuploidy evaluation is to be offered to the patient. If cfDNA is negative then no further aneuploidy evaluation is to be done in case of isolated absent nasal bone[2].

THICKENED NUCHAL FOLD

Thickened nuchal fold was described by Benacerraf et al[6] in 1987 as a very sensitive sonographic marker for Down's syndrome. It has the highest predictive value for Down's syndrome as an isolated marker. The nuchal fold is measured in the trans cerebellar plane, with thalami and cavum septum pellucidum in the same imaging plane, and measurement is taken from the outer edge of the skin to the outer edge of the bone (Fig. 2). Normal values of nuchal fold according to gestational age are <5 mm at 14-18 weeks of gestational age and < 6 mm at 19-24 weeks[7]. Studies have shown a positive correlation between nuchal fold thickness and congenital heart defects[5]. Hence, it is recommended to perform a special scrutiny of the fetal heart upon detection of an increased NF thickness. In the presence of an isolated thickened nuchal fold, there is a strong recommendation that the pregnant woman must be counselled and risk assessment and non-invasive serum screening tests or diagnostic tests for trisomy 21 are to be done, according to patient preferences and clinical scenario. In case of negative screening results and isolated thickened nuchal fold, option of cfDNA or diagnostic testing or no further aneuploidy evaluation is to be offered to the patient. If cfDNA is negative then no further aneuploidy evaluation is to be done in case of isolated thickened nuchal fold[2].

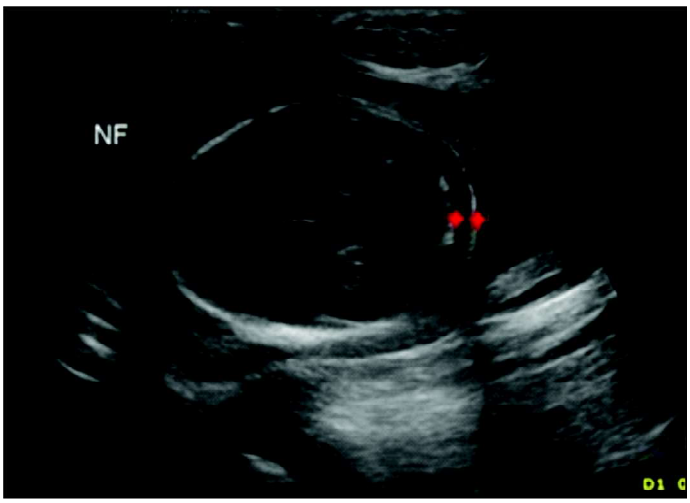

Fig. 2: 2 D gray scale ultrasound image of fetal head in trans cerebellar plane showing the correct method of measuring the nuchal fold. It is measured from outer edge of skin to outer edge of bone.

CHOROID PLEXUS CYST

Choroid plexus cysts are found in 2-4 percent of fetuses in the second trimester[4]. They have been described as small hypoechoic fluid-filled structures with well-defined walls within the choroid plexus of the lateral ventricles, mostly in the atria (Fig. 3). Isolated choroid plexus cysts are now considered as normal variants and have a good prognosis, and nearly all regress by third trimester, with no effect on neurodevelopmental outcome. However, they are associated with trisomy 18, with a high likelihood ratio when they occur in conjunction with other structural anomalies, and require evaluation for aneuploidy[2].

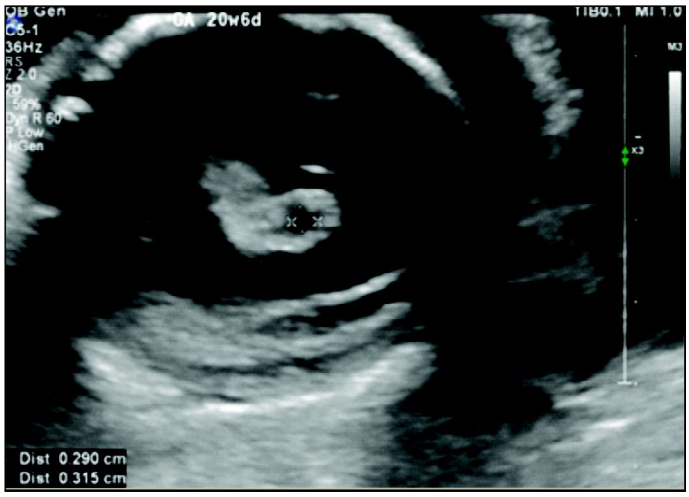

Fig. 3: 2 D gray scale ultrasound image of fetal brain showing a well-defined hypoechoic sub centimetric structure within the lateral ventricle of fetus, s/o choroid plexus cyst.

ECHOGENIC INTRACARDIAC FOCUS

It is described as a focus of increased echogenicity, as bright as the surrounding bone, seen in the heart chambers and must be visualized in at least 2 separate planes (Fig. 4). It is the most controversial among all the soft markers since it is found in about 3-5 percent of normal fetuses[2]. The most common location of the focus is the left ventricle, with a single focus being more common than multiple foci, and foci in the right ventricle more commonly associated with cardiac anomalies. In about 90% of cases, they disappear by the third trimester of pregnancy. A recently conducted meta-analysis[8] has shown the prevalence of isolated echogenic cardiac focus in 11.49% of fetuses with Down's syndrome, with a statistically significant association, although with LR of 2.68 as compared with normal fetuses indicating a small increased risk. There was no significant association with

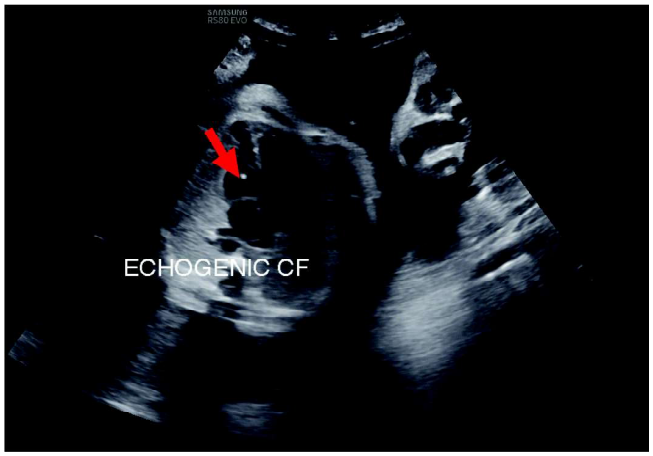

Fig. 4: 2D gray scale ultrasound images of fetal heart 4 chamber view showing echogenic intracardiac focus in left ventricle of fetus.

other structural anomalies. This is supported by the results of another meta-analysis[9] which showed that EIF could be used to identify rather than rule out Down's syndrome. The presence of echogenic intracardiac focus, therefore, is an indication for counselling and non-invasive aneuploidy evaluation, however, it does not require fetal echocardiography or follow up scans[2].

ECHOGENIC BOWEL

It is described as an echogenic area in fetal bowel greater than or equal to that of surrounding fetal bone (iliac crest) (Fig. 5). Current recommendations for its identification are a coronal view in which bowel and both iliac bones are in the same imaging plane and reducing the gain till bowel and/ or bone are not seen. To avoid false positives, it is recommended to use a lower frequency transducer (<5MHz) and adjust/ lower the gain. It has an incidence of 0.2-1.8 percent in 2nd trimester, and can be a transient or idiopathic finding in approximately 0.5% of all fetuses[2]. Multiple studies have shown its association with aneuploidy, cystic fibrosis, structural abnormalities and congenital viral infection, however, it has good outcome with most cases showing regression of echogenicity on follow up scans[10]. The outcome tends to be unfavourable if it is associated with multiple other anomalies or IUGR. Therefore, in addition to evaluation for trisomy 21, fetuses with echogenic bowel are to be reassessed on follow up scan at third trimester for evaluation of growth.

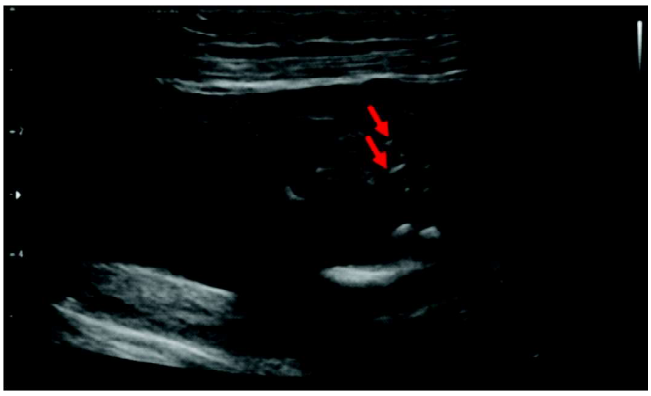

Fig. 5: 2D gray scale ultrasound image of fetal abdomen showing echogenic small bowel loops, none of the loops were dilated.

URINARY TRACT DILATION

It is described as dilation of the renal pelvis, diagnosed when the anteroposterior diameter of the renal pelvis measures ≥ 4 mm from 16-27 weeks of gestation, and ≥ 7 mm from 28 weeks of gestation[11] (Fig. 6). While often a temporary physiologic condition, it can serve as a marker for aneuploidy and could be a precursor of potential urinary tract pathology. A follow-up ultrasound should be advised at 32 weeks to rule out persistent pyelectasis.

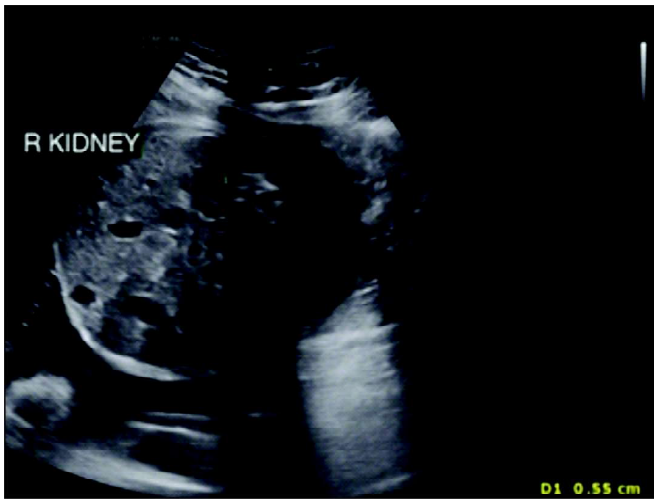

Fig. 6: 2D gray scale ultrasound image of fetal abdomen showing dilated right renal pelvis, with APD of ~5.5 mm.

SHORTENED LONG BONES

Shortened humerus and femur are defined as bone length falling below the 5th percentile for gestational age or by using the ratio of observed to expected bone length (based on biparietal diameter) for diag-nosis[12]. Short humerus and femur are associated with skeletal dysplasia and FGR and hence follow-up scans for growth evaluation are necessary. Studies have also found also found higher rates of preterm delivery and pre-eclampsia in cases of isolated short humerus and femur[13].

SINGLE UMBILICAL ARTERY

The risk of chromosomal anomaly with a single umbilical artery and associated congenital defects has been reported to be as high as 50%[2] (Fig. 7). Thus the presence of a single umbilical artery should prompt an in-depth search for other concurrent anomalies, especially involving the cardio-vascular and renal systems[14]. However, the association of chromosomal anomalies, preterm delivery, and FGR with an isolated single umbilical artery remains controversial. Some studies recommend follow-up ultrasound in the third trimester for evaluation of growth[2].

CURRENT RECOMMENDATIONS

A summary of current recommendations for evaluation of soft markers is shown in following Table 1:

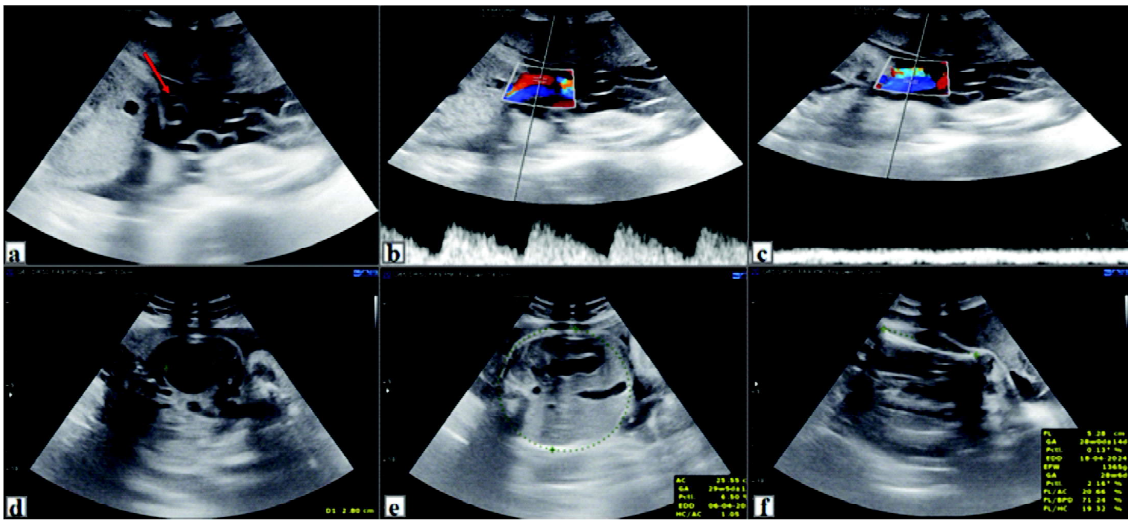

Fig. 7: This was a patient for antenatal ultrasound, 33 years, G4P4A2 at 31 weeks 4 days. 2D gray scale ultrasound image showing a) single umbilical artery (indicated by red arrow), b), c) Doppler images showing corresponding waveforms of the umbilical artery and umbilical vein, d) associated renal pyelectasis e) AC was < 10th percentile, f) FL was <3rd percentile and EFW was < 3rd percentile, suggestive of FGR. Risk assessment and non-invasive screening for aneuploidy was done, which turned out to be negative. The patient was advised follow up with Doppler.

Table 1: Current recommendations for evaluation of soft markers

#	Soft marker	Aneuploidy evaluation	Follow up scan
1.	Absent or hypoplastic nasal bone	✓ • Detailed scan to look for other soft markers/ structural defects. • Risk assessment. • Non-invasive aneuploidy screening. • Diagnostic testing, if indicated.	x
2.	Thickened nuchal fold	✓ • Detailed scan to look for other soft markers/ structural defects. • Risk assessment. • Non-invasive aneuploidy screening. • Diagnostic testing, if indicated.	x
3.	Choroid plexus cyst	✓ • Risk assessment. • Non-invasive aneuploidy screening	x
4.	Echogenic intracardiac focus	✓ • Risk assessment. • Non-invasive aneuploidy screening.	x
5.	Echogenic bowel	✓ • Look for evidence of aneuploidy, infections, cystic fibrosis. • Risk assessment. • Non-invasive aneuploidy screening	✓ • In third trimester for evaluation of fetal growth.
6.	Urinary tract dilation	✓ • Risk assessment. • Non-invasive aneuploidy screening	✓ • At >=32 weeks to decide postnatal management.
7.	Short long bones	✓ • Detailed scan to look for skeletal dysplasia and evidence of FGR. • Risk assessment. • Non-invasive aneuploidy screening.	✓ • In third trimester for evaluation of fetal growth.
8.	Single umbilical artery	✓ • Detailed scan to look for other structural defects, look at fetal heart and kidneys. • Risk assessment. • Non-invasive aneuploidy screening.	✓ • In third trimester for evaluation of fetal growth.

Table (*contd*...)

CONCLUSION

Soft markers are commonly found in routine obstetric scans and are usually associated with a low risk of aneuploidy, especially when present in isolation and screening tests are negative. However, when a multiple of these soft markers exist, they may also point towards a non-aneuploid condition, which may require a detailed evaluation.

KEY POINTS

- An isolated soft marker on ultrasound may be a transient finding.

- Must be evaluated in the context of clinical risk factors for aneuploidy and the likelihood ratio of soft marker.
- A detailed obstetric ultrasound must be done to exclude the presence of other structural anomalies.
- A cluster of soft markers may point towards a specific chromosomal anomaly.

ABBREVIATIONS USED

MoM-Multiples of median
LSCS-Lower segment Caesarean section
DM-Diabetes mellitus
HTN-Hypertension
cfDNA-cell-free DNA
NF-Nuchal fold
FGR-Fetal growth retardation
IUGR-Intrauterine Growth Restriction
LR-Likelihood ratio
AC-Abdominal circumference
FL-Femur length
EFW-Estimated fetal weight

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Prenatal Diagnosis of Down's Syndrome

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INTRODUCTION

Downs syndrome (DS) is a genetic condition due to aneuploidy (change in number) of Chromosome 21 giving rise to three copies of either the complete chromosome or of just the critical region. It is the most prevalent genetic cause leading to intellectual disability.

Down syndrome/DS can result from three different genetic conditions:

1. Non disjunction type, the most common condition where an extra chromosome 21 is present in every cell (Fig. 1)
2. Translocation, where the extra 21st Chromosome is translocated onto another chromosome.
3. Mosaicism, where the extra copy is present only in a certain percentage of the cells.

Downs syndrome is found in 1 in 700 live births[1], and is the most common autosomal chromosomal aneuploidy. Infants with Down syndrome often experience significant cognitive impairment and may also exhibit defects in other organs, such as the heart, gastrointestinal tract, eyes, and ear. Currently, there is no established cure and the treatment is supportive care to ensure quality of life. It causes profound mental, emotional, social, and economic impacts on the family as of the infants with DS, 85% survive the first year and 50% will live longer than 50 years, hence detection of DS in early pregnancy is greatly emphasized.

The likelihood of Trisomy 21 rises as maternal age increases and diminishes as gestation advances as 30% of

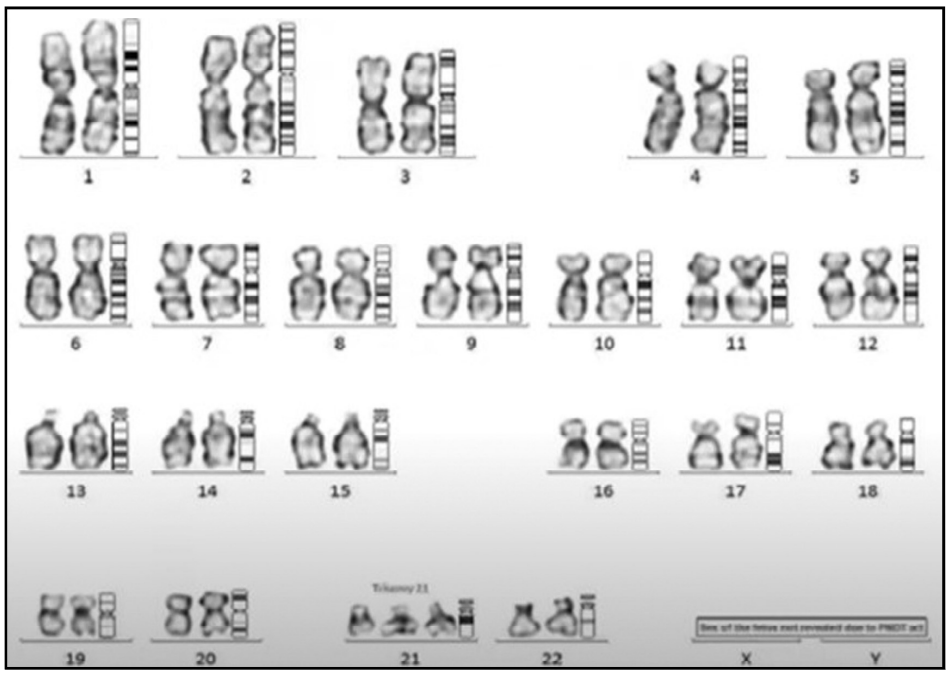

Fig. 1: Karyotype of Down syndrome (Non disjunction type)

such pregnancies fail between 12 weeks and term (Table 1). The majority of DS babies occur in babies born to women under 35 years of age, only 20-30% in women above 35 years of age. Therefore, guidelines recommend fetal aneuploidy screening in pregnant women of all ages. A screening test detects the risk of genetic disease and signals further testing for confirmation.

Table I: Prevalence of Trisomy 21 by Maternal Age and Gestational Age[2]

Maternal Age (y)	Gestational Age (WK)					
	10	12	14	16	20	40
20	1:983	1:1068	1:1140	1:1200	1:1295	1:1527
25	1:870	1:946	1:1009	1:1062	1:1147	1:1342
30	1:576	1:626	1:668	1:703	1:759	1:895
35	1:229	1:249	1:266	1:280	1:302	1:356
40	1:62	1:68	1:72	1:76	1:82	1:97
45	1:15	1:16	1:17	1:18	1:19	1:23

PATIENT SPECIFIC RISK

Every woman has an inherent risk for fetal aneuploidy which is called as A priori risk which is determined by the age and the gestational age of the woman. This A priori risk combined with risks calculated from ultrasound findings and serum biochemistry results in the pregnancy specific risk. Based on this specific risk, the pregnancy is categorized into high risk or low risk for aneuploidy and thus counselled accordingly for any further testing.

Relevant Terminology

***Screen Positive*:** Percentage of individuals who are reported positive in the screening test.

***Detection Rate*:** Percentage of affected individuals amongst those diagnosed screen positive by the test (Higher the better).

***False Positive Rate (FPR)*:** Percentage of unaffected individuals amongst those diagnosed to be screened positive by the test (lower the better).

PRE TEST COUNSELLING

Before conducting a prenatal screening test, the couple should be offered pretest counselling. The counselling should be informed and non-directive. It involves explanation about the risk of aneuploidy (A priori risk) and the need for screening. The couple should be given the options of the various tests available after explaining the mode of inheritance, detection rate, limitations of the test, and turn around time which is known as the cafeteria approach. Finally, the couple can be guided to opt for a single test and not have multiple tests performed simultaneously.

POST-TEST COUNSELLING

Post-test the couple is counselled regarding the risk of aneuploidy reported by the test and depending on the risk if further diagnostic tests or Non invasive prenatal test (NIPT) could be offered. They are counselled regarding the option to continue or opt for termination of pregnancy depending on the final test report.

Biochemical Screening

Specific serum analyses are measured as standardized Mass Units which are converted to Multiples of Median (MoM) which is gestation specific. As population based Median values are different for different gestational ages this is a simple way to assess an individual's risk in the context of the entire screened population. Since it is gestational age based the dating should be accurate (done most accurately by CRL at 11-13^{+6}).

1. ***First Trimester Biochemical Screening*:** The maternal serum markers valued in the first trimester are free Beta human chorionic gonadotropin (beta hCG) and pregnancy associated plasma protein A (PAPP-A). It is performed between 11 and 13^{+6} weeks. (Table 2)

Table 2: Expected biomarker levels in euploid and aneuploid fetuses[3, 4]

Study Population	Median free beta hCG (MoM)	Median PAPPA (MoM)
Euploid	1.0	1.0
Trisomy 21	2.0	0.5

2. ***Second Trimester Biochemical Screening*:** It is done between 15 – 20 weeks of gestation. The serum markers measured are - Maternal serum free beta hCG, Unconjugated estriol, Alpha-fetoprotein (AFP), and Inhibin-A, known as the "Quadruple screen". (Table 3). Earlier Triple marker which comprised of 3 serum analytes except Inhibin A being done in second trimester has been abandoned due to low sensitivity as compared to Quadruple test.

Table 3: Serum Analytes in Down Syndrome.

Serum marker	Trisomy 21	MoM values
uE3	Decreased	0.73 or less
AFP	Decreased	0.75 or less
Free B hCG	Increased	2.05 or more
Inhibin	Increased	2.10 or more

ULTRASOUND SCREENING

1. ***First Trimester Ultrasound*:** It is performed when CRL (Crown Rump Length) is between 45 – 84mm (11 – 13^{+6} weeks) and is an important tool for screening for

aneuploidy along with other single gene disorders. The parameters evaluated are: Nasal Bone, Nuchal Translucency, Ductus venosus, and Tricuspid Regurgitation. According to a study by the Fetal Medicine Foundation, screening for trisomy 21 with nuchal translucency had a detection rate (DR) of 77% with a 5% false-positive rate (FPR) [5]. Absent nasal bone is seen in 73% of fetuses with DS, with a FPR of 0.5%[6]. An abnormal ductus venosus waveform has a 67% sensitivity with a 5% FPR for trisomy 21[7]. The best time for testing the serum markers is at 10 weeks while the Nuchal scan has the best detection rate at 12 weeks or more however for reducing the number of visits and optimal results both serum markers and the NT scan is recommended to be done at 12 weeks (combined first trimester screen). (Fig. 2)

2. ***Second Trimester Ultrasound*:** All pregnant women should undergo a comprehensive anatomical ultrasound between 18 and 22 weeks of gestation to identify any structural abnormalities and soft markers. Soft markers are normal anatomic variants that confer an increased risk of aneuploidy. When used alone, second trimester ultrasound is the least effective screening method for screening as only 8.5% of fetuses with trisomy 21 have major structural anomalies as per the FASTER trial[4]. Cardiac defects and duodenal atresia are the most common malformations found in Trisomy 21.

APPROACHES TO ANEUPLOIDY SCREENING

Integrated Screen

Antenatal woman undergoes the first trimester combined screening and following that second trimester serum analytes. She receives a common result after the second trimester test. If only serum screening is done in both trimesters without NT and NB, it is known as an integrated serum screen. In this test, it is important to counsel the patient that results will be only available after the second trimester screening, and high risk women who want results earlier can opt for a different test.

PREGNANCY DETAILS

Fetuses: 1		**EDD:**	10-08-2019	**Age of term:**	34
GA is based on:	CRL67 mm at 02-02-2019	**LMP Date:**	06-11-2018	**LMP Certainly:**	Regular Cycle
Fertilization Date:	17-11-2018	**Smoking:**	None	Insulin Dependent Diabetes	
Previous Down's	Previous Edwards'	Previous Patau's		Previous CdLS	
Previous SLOS	Previous Tiploidy	Previous Tumer's		Previous NTD	

SPECIMEN DETAILS

Barcode:	LI190011491	**Collector:**							
Collected:	02-02-2019	**Gest. at Coll date:**	13 Weeks 0 Days	**Received:**	04-02-2019	**Weight:**	95 kg		
Scan Date:	02-02-2019	**Gest. at scan date:**	13 Weeks 0 Days						

CRL	**CRL2**	**BPD**	**BPD2**	**HC**	**HC2**
67 mm					

Test Name	Conc.	Unit	CorrMom
hCGb	19.68	ng/mL	0.79
NT	1.6	mm	0.97
PAPP-A	1040.00	mU/L	0.53

RISKS

Disorder:	**Down's syndrome**			**Result:**	**Low**
Final risk:	1:8315	**Age risk:**	1:522		
Cutoff:	1:250	**Risk type:**	Risk At Term	**Status:**	Signed
Disorder:	**Edward's syndrome**			**Result:**	**Low**
Final risk:	1:96050	**Age risk:**	1:4397		
Cutoff:	1:100	**Risk type:**	Risk At Term	**Status:**	Signed
Disorder:	**Patau's syndrome**			**Result:**	**Low**
Final risk:	1:86786	**Age risk:**	1:14099		
Cutoff:	1:100	**Risk type:**	Risk At Term	**Status:**	Signed

PLEASE NOTE:
This interpretation assumes that patient and specimen details are accurate and correct. In all case where and assessment of increased risk is based on LMP dates, the gestational age must be by ultrasound before further action is taken. It must be clearly understood that the results represent risk and not diagnostic outcomes. Increased risk does not mean that the baby is affected and further test must be performed before a firm diagnosis can be made. A low risk result does not exclude the possibility of Down's syndrome or other abnormalities, as the risk assessment does not detect all affected pregnancies. Lilac Insights does not bear responsibility for the NT result. The company strongly recommends that only NT value from qualified experts (for example, clinicians certified by the Fetal Medicine Foundation) is utilized to provide a 1st trimester risk. These results were analyzed with Lifecycle software from PerkinElmer Life and Analytical Sciences & Final report generated from 21st Century Informatics BV.

Fig. 2: Sample report of combined first trimester screen

Sequential Screening

The result of the combined first trimester screen is disclosed to the woman allowing for earlier confirmatory testing if needed. If the result of first trimester screening is low risk, they are informed and the second trimester serum screening is done after which the final risk is calculated.

Contingent Screening

In contingent screening, pregnancy is categorized into high risk, intermediate risk, and low risk as per the results of first trimester screening. High risk women are given option of invasive testing or NIPS. Low risk women are counselled for no additional screening. Intermediate risk group undergoes screening in 2nd trimester and a combined final risk is calculated. Contingent screening has a higher detection rate with lower false positive rates (Table 4). First trimester and second trimester screening are not performed as unlinked tests as that leads to higher false positive rates

Maria Agathekolous conducted a meta-analysis that includes an Excel sheet for calculating the risk of aneuploidies depending on the occurrence or non-appearance of multiple soft markers. The common soft markers associated with DS are Ventriculomegaly, echogenic bowel, short long bones, absent nasal bone, and thickened Nuchal fold both in first and second trimester (Table 5). Other calculators are freely available online on different websites related to fetal medicine for calculating the final risk after adding the required information.

Interpretation of Combined first trimester screen (AOGD Fetal medicine subcommittee recommendation)

> 1: 250 - High risk or screen positive for Aneuploidy. Pretest counseling and invasive testing for aneuploidy should be offered.

1:250-1:1500 - Intermediate risk. Pretest counselling and option for Integrated serum test if available or contingent screen with Non invasive prenatal test.

< 1: 1500 - Low risk. No further testing required.

Non Invasive Prenatal Screen (NIPS)

Maternal blood contains cell-free fetal DNA, which is utilized for detecting aneuploidy. It can be performed after 9 weeks of gestation till term. The main benefit of NIPT is the safety with the highest sensitivity of 99.4% in screening for DS and invasive procedures may be avoided. NIPS can be offered in

- Age 35 years or older
- Ultrasound features suggesting increased risk of aneuploidy
- History of trisomy 21 in previous pregnancy
- Positive Combined screening tests/ Quadruple test.
- Parental balanced Robertsonian translocation involving chromosome 13, 18 or 21.
- Contingent NIPS can be implemented in routine clinical practice after pretest counselling.

Table 4: Approaches to Aneuploidy Screening[7]

Screening Approach	Pog	Markers	Detection Rate For Trisomy 21 (%)
Nuchal Translucency scan	11–13 6/7	NT	70 FPR: 5%
Dual marker	11–13 6/7	PAPP-A and Beta HCG	70 FPR: 5%
Combined test	11–13 6/7	1. Maternal age 2. PAPP-A and Beta HCG 3. NT	82-87 FPR: 5%
Combined test with NB/ TR/DV	11–13 6/7	Combined test + NB/ TR/ DV	93-96 FPR 2.5%
Expanded first trimester screen	11–13 6/7	1. Maternal age 2. PAPP-A and Beta HCG 3. NT 4. NB 5. PIGF	DR: 98% FPR: 1.2%
Quadruple screen	15–22 weeks	1. AFP 2. uE3 3. Beta HCG 4. Inhibin A	81 FPR:5%
Full integrated test	10–13 6/7 and then 15–22	1. NT and PAPP-A 2. AFP, uE3, bHCG Inhibin A First trimester results not provided	96
Sequential stepwise	10–13 6/7 and then 15–22	1. PAPP-A 2. AFP, uE3. bHCG Inhibin A First trimester portion of integrated screen provided High risk – offer CVS / NIPT Low risk – proceed with second trimester screening	95
NIPS	9-10 week to term	Cell free fetal DNA	99

Table 5: Likelihood ratio of soft markers for trisomy 21[8]

Marker	LR+	LR-	LR isolated
Echogenic intracardiac focus	5.83	0.8	0.95
Ventriculomegaly	27.52	0.94	3.81
Increased NFT	23.3	0.8	3.79
Echogenic bowel	11.44	0.9	1.65
Mild Hydronephrosis	7.63	0.92	1.08
Short Humerus	4.81	0.74	0.78
Short Femur	3.72	0.8	0.61
ARSA (aberrant right subclavian artery)	21.48	0.71	3.94
Absent/Hypoplastic NB	23.27	0.46	6.58

Minimum fetal fraction required to report the test is 4%. Women with results not reported, indeterminate, or uninterpretable (a "no call" test result) from NIPS should undergo further genetic counselling and offered careful ultrasound assessment and invasive testing. Chromosomal mosaic placenta may not be detected by NIPS. Currently, it is validated only for five chromosomal aneuploidies i.e. 13, 18, 21, and Gonosomes (X and Y). NIPS should not be offered for any other fetal condition such as structural anomalies.

Screening for DS in Multiple Gestation

It does not apply to higher order pregnancies. Combining maternal age with nuchal translucency is an effective method for aneuploidy screening in multiple gestation, with a detection rate (DR) of 75% with a false-positive rate (FPR) of 5%. Chorionicity is essential for screening and in dichorionic gestation, the risk is assessed per twin, whereas in monochorionic, it is calculated per pregnancy. NIPT can be offered in twin pregnancy however the risk will be per pregnancy and not fetus.

Confirmatory Tests / Invasive Tests

If the screening test is high risk for DS, the couple can be offered Chorionic villous sampling (CVS) or amniocentesis.

1. ***Chorionic Villous Sampling (CVS)*:** CVS involves collecting a sample from the placenta for genetic diagnosis between 10-13 weeks gestation and is an outpatient procedure. The most serious risk with CVS is of abortion and limb defects in the fetus. In experienced hands, the rate of pregnancy loss is low (0.1–0.3 %). Disadvantage of CVS is that it cannot diagnose Confined placental Mosaicism.
2. ***Amniocentesis*:** Amniocentesis is the most common prenatal invasive diagnostic test performed and involves withdrawing amniotic fluid from the uterus for genetic studies. It should be performed at>16 weeks gestation. The procedure-related loss is quite low (0.01–0.3 %).
3. ***Cordocentesis*:** It is percutaneous umbilical blood sampling and is performed by puncturing the umbilical vein to obtain fetal blood cells. The pregnancy loss rate is quite high (1-3%) and is therefore only used for genetic testing.

CONCLUSION

Down syndrome can be suspected during early pregnancy by various screening methods and confirmed by invasive genetic techniques. It offers the couples the advantage of early termination of pregnancy, less medical complications, reduced economical burden to health system and reduced emotional impact on couples.

KEY POINTS

1. Combined first-trimester screening test is the most effective screening test for Down Syndrome which includes the measurement of nuchal translucency, maternal age, and serum analytes.
2. The obstetrician's role is to offer counselling about the risk of Down Syndrome in each pregnancy.
3. Pre and post-test counseLling is crucial to ensure that the couple understands the process and results of the test.
4. The Non-Invasive Prenatal Test (NIPT) serves as a screening test and should be followed up with an invasive test for confirmation. Its negative predictive value is 99.4% for DS.
5. It is advisable to refer the couple to a Geneticist or fetal medicine specialist for risk assessment and counselling. Decisions regarding pregnancy termination should not be based solely on screening test results.

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Doppler in Management of Fetal Growth Retardation

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INTRODUCTION

Foetal growth restriction (FGR) is defined as the failure of the foetus to reach its genetically determined growth potential. The pathophysiology of FGR is far from simple, and it is usually attributed to the process of inadequate oxygenation and insufficient placentation. Nearly 50% of preterm and 20% of term perinatal mortality is attributed to this phenomenon.[1]

In utero growth restriction is not just associated with mortality but also entails significant perinatal morbidity that has implication well into adulthood in the form of metabolic syndrome, cardiovascular risks and neurodevelopmental complications.[2, 3, 4]

Since, blood flow reaching the fetus through the umbilical vasculature, its source from the uterine vessels and its redistribution within the fetus to vital organs such as the cerebral circulation have important role to play in the screening, diagnosis, surveillance of FGR, Doppler investigation of these vessels has vital importance in managing pregnancies affected by this menace.

DOPPLER INDICES

The doppler interrogation of vessels leaves us with multiple indices such as the resistance index, the pulsatility index, the systole to diastole ratio (S/D ratio) and the peak systolic (PS) and end diastolic (EDV) and mean velocities (MV) which are the basis for calculation of these indices. It is imperative to understand these indices to determine why the pulsatility index has been chosen as the index in the consensus definition of FGR. Fig. 1 lists the formulae used to derive the three major indices used in Obstetric Dopplers. The Pulsatility index as shown, takes into account the average velocity of the waveform rather than extreme values of peak systole or end diastole. So, its value does not reach infinity even in cases of severe FGR.

$$\text{Pulsatility index} = \frac{\text{Peak systolic velocity} - \text{End diastolic velocity}}{\text{Time averaged maximum velocity}}$$

$$\text{Resistance index} = \frac{\text{Peak systolic velocity} - \text{End diastolic velocity}}{\text{Peak systolic velocity}}$$

$$\text{Systole / Diastole ratio} = \frac{\text{Peak systolic velocity}}{\text{End diastolic velocity}}$$

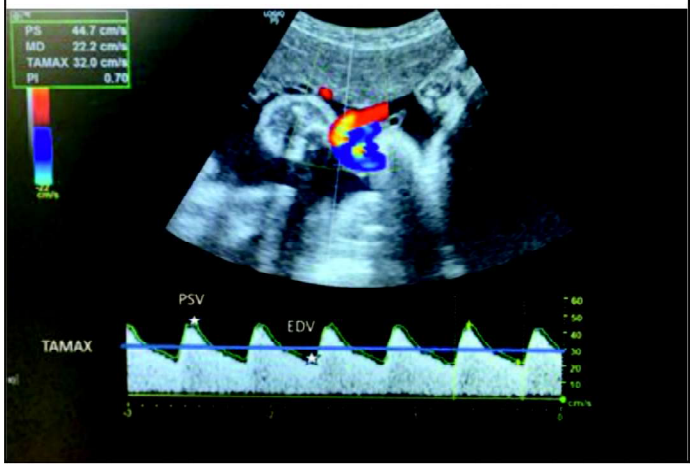

Fig.1: Doppler Indices

PREDICTION OF FGR

Uterine artery PI as part of first trimester scan of pregnancy has been studied for its predictive value for the development of FGR. However, the detection rate of for preterm FGR is 64% and that of term FGR 20% for a false positive rate (FPR) of 10%.[5] Another systematic review and meta-analysis on the subject found that mean uterine artery PI was significantly high for women with FGR fetuses through pregnancy in all trimesters.[6]

Thus, while scientific literature is endowed with association of uterine artery doppler with development of FGR, the performance of screening even when used as a marker along with other maternal historical factors remains far from efficient.

DISTINGUISHING FGR FROM SGA

If the definition of failure to reach growth potential is taken as the definition of FGR, and the growth is identified using size alone, then the criteria used is estimated fetal weight less than the 10th centile. However, this subset is likely to include fetuses who are constitutionally small and therefore not at a higher risk of neonatal jeopardy. In order to distinguish this subset from those with pathological growth restriction the consensus definition of FGR has now included doppler abnormalities as an essential part of the diagnosis if the EFW/ AC are between 3rd and 9th centile. (Refer section 5 for details) [7]

Recent literature comparing the performance of the two different criteria of FGR for their association with adverse perinatal outcome conclude that the definition including doppler indices in addition to foetal size are more specific for adverse perinatal outcomes. This leads to better utilization of resources for surveillance and reduced parental anxiety.[7]

DIFFERENTIATING EARLY AND LATE ONSET FGR

The entity of FGR has been known in medical literature since a very long time. However, the precise definition of FGR has been a matter of constant debate. The Delphi consensus, 2016 by Godjin et al is a historical research article that has changed the way FGR is defined; and ACOG, SMFM and FIGO have now endorsed in their respective guidelines, this definition put forth.[5, 8-10]

As per this definition, a foetus growing extremely small (Abdominal circumference/ estimated foetal weight less than third centile) is classified as FGR. In the event that smallness is less severe as in AC/ EFW < 10th centile, the smallness has to be accompanied by Doppler changes in either the Uterine artery (Ut A PI > 95th centile) umbilical (Umbilical Artery pulsatility index of > 95th centile), in case of early onset FGR, meaning thereby that high resistance in the uteroplacental circuit has been quantified. This high resistance renders part of the placenta incompetent for gas and nutrient exchange. Thus, with deteriorating placental function there is sequential worsening of umbilical artery doppler, ie, Umb A PI > 95th centile (30% placental villous dysfunction), absent end diastolic flow (50% mal-perfusion of villous vasculature) and reversed end diastolic flow 70% not available. This is followed by sequential deterioration in venous side with DVPI > 95th centile and reversed a wave in DV. These chronological changes reflect worsening perinatal outcome.

In late onset FGR, since the umbilical artery is not always affected in as much magnitude as in early onset, but more often there is more subtle affliction, the cerebroplacental ratio < 5th centile is used to define late onset FGR. The cerebroplacental ratio is a ratio of middle cerebral artery PI to umbilical artery PI. In cases of late onset fetal compromise (> 32 weeks), the placental dysfunction is often less than that required to escalate the umbilical artery PI to more than the 95th centile. Also, the fetus as a compensation, resorts to redistribution of blood flow to vital organs such as the brain, by reducing the resistance to these areas. This is reflected in a fall in the MCA PI. In order to identify this worsening in both the uteroplacental and the fetal compartments early on, the CPR is used to define late onset FGR. The CPR being a ratio of both these entities tends to worsen sooner than its individual components.

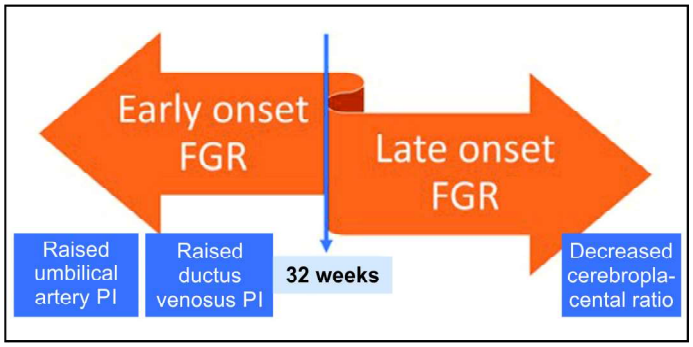

Fig. 2: Differentiating between early and late onset FGR

It is important to differentiate early from late onset FGR since the natural history of these disorders and the clinical challenges they pose are significantly different from one another (Fig. 2). Early onset growth restriction is easily diagnosed clinically with discordance between period of gestation and symphysio-fundal height. These pregnancies are render themselves to with predictable follow up with worsening in umbilical artery followed by DV. Here, the challenge is to secure a balance between preterm birth and ongoing in utero fetal compromise.

The late onset FGR on the other hand has babies who are not necessarily low birth weight. Hence clinically they may not appear growth restricted. Serial ultrasound can trace their journey from SGA to FGR with falling quartiles. Also, including centiles in biometry indices can pick up babies with EFW/ AC less than 3rd centile or those with parameters less than 10th centile but falling CPR. These are the babies who have poor reserve to tolerate the in utero hostile environment and thus tend to deteriorate very suddenly as opposed to the gradually developing compromise in the early onset variety. Most importantly, missed late onset growth restriction is the most common underlying cause of unexplained stillbirths.

SURVEILLANCE

The uterine and umbilical dopplers combined help assess the uteroplacental function in pregnancy (Table 1). The fetal

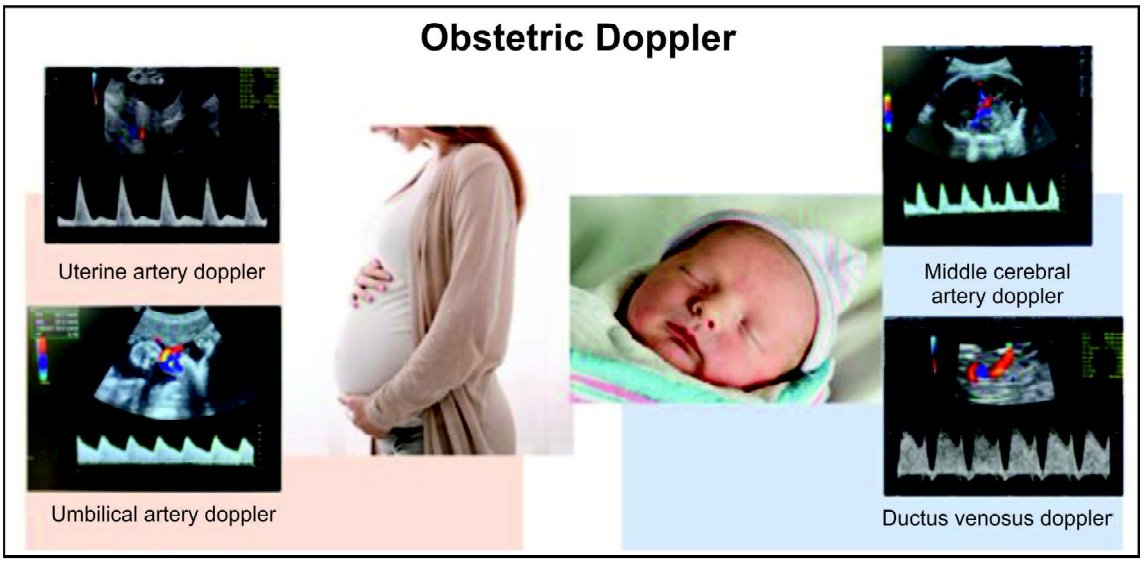

Fig. 3: Dopplers depicting feto-maternal pathology

dopplers such as middle cerebral artery doppler and ductus venosus doppler reflect the foetal cardiovascular adaptation in the face of adverse uterine milieu suggestive of hypoxia and eventually acidosis. (Fig. 3)

Table 1: Role of different vessel dopplers in identifying uteroplacental / fetal pathology

Vessel	*Pathology*
Increase Uterine artery PI (Ut A PI)	Lack of physiological trophoblastic invasion of spiral arterioles
Increased Umbilical artery PI (UA PI)	Reduced functional area of the placental available for exchange of gas and nutrients + Increased cardiac afterload of the foetus
Decreased Middle Cerebral artery PI (MCA PI)	Foetal cerebral vasodilatation reflecting brain sparing in the face of fetal compromise
Incrased Ductus venosus PI (DV PI)	Increased atrial pressure suggestive of an increasing cardiac afterload commensurate with increasing placental resistance

Early onset FGR

The probability of fetal jeopardy is reflected in Umbilical artery PI which is a surrogate marker for placental mal-perfusion. Hence, the degree of compromise determines the frequency of monitoring. Thus, with a baby diagnosed as early onset FGR, and umbilical artery PI > 95th centile, repeat doppler interrogation should be planned on weekly basis. Once AEDF has set in, cardiovascular deterioration is likely in a median time interval of five days and the odds ratio for the outcome of stillbirth is 3.6 (2.4-5.5). With AEDF, the frequency of monitoring increases too twice weekly. With REDF, further deterioration is anticipated in 2 days and OR for stillbirth is 7.3 (4.5-11.4). Here, the patient must be reviewed with repeat doppler at least every alternate day. In practice, patients with AEDF and worse are frequently hospitalized, hence, monitored more closely. [1]

Late onset FGR

Late onset FGR is associated with more subtle placental dysfunction, as discussed earlier. Also, the fetus with this condition is less resilient to hypoxia and therefore the window of opportunity to act is limited. Failing to act within the stipulated time predisposes to stillbirths in cases of late onset FGRs. Keeping these two ideas in mind, for monitoring, the cerebro-placental ratio is used, since this picks up the fetal compromise before its individual components, the umbilical or MCA PI. In the event of a low CPR (< 5th Centile)

The doppler should be repeated 24 hours late to confirm the findings to avoid false positives, especially when this determines the time to deliver. If the UA PI is > 95th centile, weekly monitoring with doppler is indicated. If the MCA PI is less than the 5th centile, it suggests compensatory mechanisms at play and there are studies to suggest that with a low MCA PI the median time to foetal deterioration was as little as five days. Thus, more frequent monitoring is indicated with biophysical profile and non-stress test. Stage based management of FGR reflects these concepts.[1]

DETERMINING TIME OF BIRTH

The time of birth is determined by the degree of in hostile in utero environ and the gestational age of the ferus. The 2020 SMFM recommendation suggests that with a diagnosis of SGA (EFW 3rd to 9th centile with normal dopplers), the pregnancy should be terminated between 38 and 39 gestational weeks.

In case of early onset fetal growth restriction, the management is stage based as given in Table 2 below.[1]

Table 2: Dopplers in surveillance / time of birth early onset growth restriction

Stage	Pathology	Criteria	Frequency of monitoring	GA/mode of birth
Stage 1	Extremely small fetus/ mild degree of placental insufficiency	EFW / AC <3rd centile or EFW / AC 3-9th centile with UA PI / Ut A PI > 95th centile	Weekly	37 weeks Induction of labor
Stage 2	Severe degree of placental insufficiency	UA AEDF	Twice a week	34 weeks By caesarean section
Stage 3	Weak suspicion of fetal acidemia	UA REDF	Daily	30 weeks By caesarean section

It is imperative to emphasize here that while doppler changes in early onset FGR, namely sequential deterioration in umbilical artery circuit from raised UA PI to REDF through AEDF and subsequent monitoring with DV dopplers is an established practice, the TRUFFLE trial suggested that when the only modality of follow up was doppler, the stillbirth rate rose by four times when compared to a combination of UA doppler plus and computerised CTG (cCTG). While cCTG is not currently available in most centres, including BPP and NST to base delivery decisions yields significantly better outcomes. It may be noteworthy, that absent 'a' wave on DV was the premise to trigger birth in only 10% of cases in the TRUFFLE trial.[11]

In so far, as the mode of delivery is concerned, the success rate of induction remote from term and the fetal reserve to tolerate the stress of labour are two factors that need to be considered. Hence, beyond stage 1 FGR, induction is unlikely to result in successful vaginal birth and is therefore not recommended. (Table 2)

Table 3: Doppler in surveillance / time of birth Late onset growth restriction[7]

Criteria	Surveillance	Time and mode of birth
EPW / AC < 3rd centile normal liquor and dopplers	Weekly CPR Biometry every two weeks NST/ BPP twice a week	36-38 weeks Induction of labor permissible
FGR with mild doppler changes UA PI > 95th centile MCA PI < 5th centile CPR < 5th centile Ut A PI > 95th centile	Consider admission Steroids for FLM if indicated as per period of gestation Biometry every two weeks Doppler of UA, MCA and twice a week BPP / NST twice a week	34-37 weeks Induction of labor permissible

The criteria to determine delivery decisions are less clear for late onset FGR given the fact that there are no randomised control trials for the same and are highly unlikely to be ever designed. The table below gives details of surveillance and decision to deliver for late onset FGR (Table 3).

Absolute doppler criteria for delivery are not as established in late onset FGR as are for early onset. The most common indications for termination of pregnancy in clinical practice include gestational age (never beyond 38 weeks), abnormalities of NST/ BPP.

EFFECT OF STEROIDS ON OBSTETRIC DOPPLERS

Administration of corticosteroids for fetal lung maturity is known to increase blood flow across the umbilical and fetal vascular circuit. This results in transient improvement in the UA PI and MCA PI. This increase, however, is not a reflection of decrease in placental vascular resistance but vasodilatation secondary to corticosteroid administration. This transient improvement should not be implied as an improvement in fetal status. On a more practical note, the absence of transient improvement after administration of corticosteroids must be viewed with concern as it is predictive of subsequent fetal deterioration.[12]

Current evidence supports the use of corticosteroids when indicated as per gestation and anticipated time of delivery, in all cases of FGR.[13]

CONCLUSION

FGR is one of the leading causes of fetal morbidity and mortality. USG Doppler study of the feto-maternal circulation is an important diagnostic modality for screening , diagnosis and further surveillance of these pregnancies to optimize outcomes.

KEY POINTS

1. Pulsatility index is the index of choice to assess Obstetric dopplers in FGR.
2. First trimester mean uterine artery PI can be used to predict early onset FGR in conjunction with maternal historical factors, and biochemical markers. The detection rate of first trimester mean uterine artery PI for preterm FGR is 64% and that of term FGR 20% for a false positive rate of 10%.
3. Doppler evaluation of the umbilical, uterine and middle cerebral artery can be used to distinguish between constitutionally small babies and pathological FGR.
4. Obstetric doppler evaluation serves to distinguish between early onset (< 32 weeks) and late onset FGR

(first identified after 32 weeks) which have differing pathophysiological and clinical trajectories.

5. Sequential worsening of umbilical vascular resistance followed by ductus venosus 'a' wave changes should be used for surveillance in early onset growth restriction.
6. UA PI, MCA PI and CPR centiles should be used for the surveillance of late onset FGR
7. Decision to deliver must incorporate findings of NST and biophysical profile in addition to Doppler indices.
8. Antenatal steroids transiently improve blood flow in umbilical and fetal arterial vasculature. This should not form the basis of decision making in FGR.

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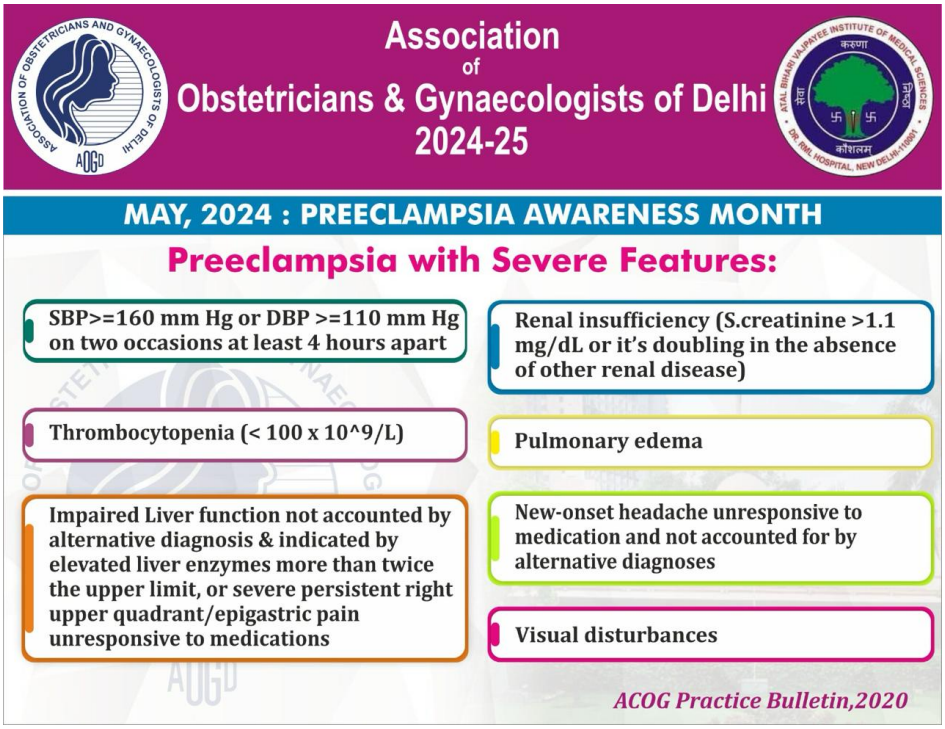

Radiofrequency Ablation in Complicated Monochorionic Twins

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INTRODUCTION

Monozygotic or 'identical' twins are formed when a single, fertilized ovum divides into two. If this division occurs within 72 hours of fertilization, dichorionic diamniotic (DCDA) twins are formed wherein there are two embryos, two amnions and two chorions. If this division occurs between the fourth and eighth days, *monochorionic* diamniotic (MCDA) twins are formed. Monochorionic twins share a single placenta and will universally have vascular anastomosis (Fig. 1), which puts these pregnancies at a higher risk of adverse outcomes due to unique complications such as Twin-to-Twin Transfusion Syndrome (TTTS) and Selective Intrauterine Growth Restriction (sFGR). These twins are also at a higher risk of being discordant for structural abnormalities. The perinatal mortality in monochorionic twins is significantly higher at 11.6% than the reported 5% in dichorionic twins[1]. Radiofrequency ablation (RFA) is a minimally invasive surgical procedure used to manage complications in monochorionic pregnancies. RFA offers a therapeutic approach to selectively reduce one fetus to improve the outcome for the remaining fetus and the mother.

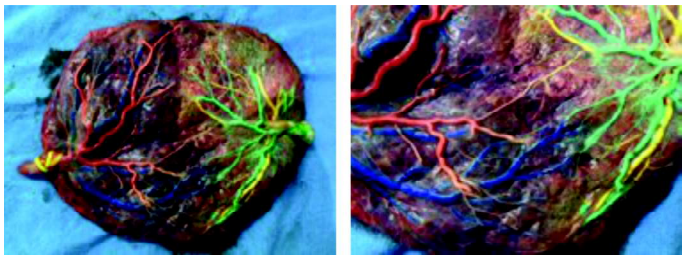

Fig. 1: Vascular anastomoses in monochorionic diamniotic (MCDA) twin pregnancy

INDICATIONS FOR RFA

RFA is usually performed between 14-28 weeks' gestation in the following complicated monochorionic twin pregnancies:

1. Severe Twin-to-Twin Transfusion Syndrome (TTTS) not amenable to or failing laser therapy.
2. Significant Selective Intrauterine Growth Restriction (sIUGR) with abnormal Doppler studies suggesting a poor prognostic outlook for one twin.
3. Twin Reversed Arterial Perfusion (TRAP) sequence, where one fetus acts as a "pump twin" for a non-viable "acardiac twin."
4. Complications in higher-order monochorionic multiples that put the pregnancy at risk.

CONTRAINDICATIONS

1. Threatened miscarriage
2. Prelabour premature ruptue of membranes (PPROM)
3. Preterm labour/cervical dilatation
4. Gestation more than 28 weeks
5. Maternal conditions that preclude the safe use of local or general anaesthesia.
6. Infections at the proposed site of entry
7. Uncontrolled maternal coagulopathy
8. Severe placental or fetal anomalies that render the procedure technically unfeasible or unlikely to succeed.

TECHNIQUE

1. ***Pre-procedural Assessment*:** A detailed ultrasound is performed to assess fetal anatomy and placental position and identify the umbilical cord insertion in the target

fetus. Cervical length is assessed transvaginally to assess the risk of preterm labour and the need for cerclage.

2. ***Informed consent*:** The couple should undergo detailed pre-procedure counselling, and informed consent should be obtained prior to the procedure.
3. ***Pre-procedure medications*:** Oral nifedipine 10 mg is given half an hour before the tocolysis procedure. A single-dose antibiotic (usually 3rd-generation cephalosporine) is also given to minimise the risk of infection. If the procedure is performed at a gestation of more than 26 weeks, a single course of antenatal steroids, dexamethasone, is given to the patient.
4. ***Anaesthesia*:** RFA is performed as a daycare procedure under local anaesthesia. Prior to RFA needle insertion, 1% xylocaine is infiltrated into the skin of the maternal abdomen. Maternal sedation can be given if the mother is uncomfortable.
5. ***Needle Insertion*:** A stab incision is given on the maternal abdomen at the selected site of entry. Under continuous ultrasound guidance, a 17G Starburst radiofrequency needle electrode is inserted through the maternal abdomen and uterus into the target amniotic sac and positioned into the target fetus close to the umbilical cord insertion.
6. ***Radiofrequency Energy Application*:** Radiofrequency energy is applied to coagulate the blood in the target vessels, ie, the umbilical arteries of the target fetus, ceasing blood flow to the selected fetus. RFA uses high-frequency alternating current to produce very high temperature within the 2 cm area of coagulation, leading to tissue necrosis. A target temperature of 100 degree Celsius is achieved and then maintained for 3 minutes; this constitutes one cycle of RFA. Care must be taken to ensure that all prongs of the needle are within the target fetus prior to starting the ablation. Coagulation is usually complete in 1-3 cycles. Colour flow Doppler is used to ensure a complete cessation of blood flow in the target fetus's umbilical cord prior to the withdrawal of the RFA needle.
7. ***Post-procedural monitoring*:** The fetal heart rate of the adjacent fetus(es) is monitored intermittently during the procedure. The main aim of the ablation is to coagulate the umbilical arteries in the target fetus in the shortest possible time so as to minimise sudden hypotension in the adjacent fetus that may occur if coagulation is delayed. Post-procedure MCA PSV should be documented to ensure that this has not occurred. This should be done immediately post-procedure and then at 24-48 hours post-procedure.
8. ***Post-procedure follow-up*:** Follow-up ultrasound to assess the wellbeing of the surviving co-twin is performed after 24-48 hours, then after a week and then 4 weekly or as clinically indicated. Fetal MRI is offered 6 weeks post-procedure or at 28-32 weeks whichever is later, to assess any evidence of cerebral injury to the co-twin. Antenatal management of the mother remains unchanged. Delivery is planned at term. Induction and/or caesarean are performed for usual obstetric indications.

COMPLICATIONS

Complications associated with RFA include

1. Miscarriage
2. Preterm labour and preterm premature rupture of membranes (PPROM)
3. Bleeding or hematoma at the needle insertion site
4. Infection
5. Co-twin demise
6. Thermal injury to the non-targeted fetus(es)
7. Risk of neurological injury to surviving co-twin

OUTCOMES FOLLOWING RFA

The reported live birth following RFA varies between 70-80% in published literature.[1-4] The commonest complication is PPROM and preterm delivery or miscarriage. The risk of cotwin demise is about 5-10%. The median gestational age at delivery following the procedure is 34-36 weeks. The median interval between procedure to delivery is reported to be around 12 weeks. There have been no reports of any serious maternal complications following RFA in published literature.

Comparison with other techniques for selective reduction in complicated monochorionic pregnancy

RFA is often compared to other techniques such as fetoscopic laser photocoagulation and bipolar cord coagulation (Table 1). While fetoscopic laser therapy is considered the gold standard for TTTS, RFA provides an alternative in cases where laser therapy is not feasible or has failed. Compared to bipolar cord coagulation, RFA is technically easier and offers a more controlled and precise ablation of the target vessels.

Table 1: Compares outcomes following selective reduction with RFA and bipolar cord coagulation.[4]

Parameter	*BCC*	*RFA*
Mean GA at procedure (weeks)	20.9 + 2.7	20.2 + 2.2
Median GA at delivery (weeks)	34.7	33
Procedure to delivery interval (days)	87.1 + 42.1	73.8 + 47.2
Overall survival (%)	85.2	70.7
PPROM (%)	27.3	13.7

CONCLUSION

Radiofrequency ablation is a valuable tool in the management of complicated monochorionic pregnancies. Its use requires careful consideration of the indications, contraindications, and potential complications. When performed by experienced operators, RFA can significantly improve pregnancy outcomes in carefully selected cases. Ongoing research and technological advancements will likely expand its applications and efficacy in fetal medicine.

KEY POINTS

1. Monochorionic twins are at risk of multiple complications.
2. RFA is an easier and precise technique for ablating target vessels
3. RFA is performed at 14-28 weeks
4. Surviving co-twin needs serial ultrasound monitoring

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Placental Rejuvenation – A Novel Strategy

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INTRODUCTION

Human placenta formed during pregnancy is a temporary endocrine organ. It produces hormones to maintain pregnancy and fetal development. It is a store house of many biologically active components like enzymes, amino acids, peptides, polydeoxyribonucleotide (PDRN), vitamins, trace elements, growth factors and multipotent cells.[1] This multipotent composition of placenta and availability of various components and functions has attracted researchers for a long time to use it as a source of biological material. It is easily available which would be otherwise discarded, healthy donor screening possible and exact age documented makes it practical to be used clinically. Stem cells can be derived from embryonic cells from blastocyst of human embryo post invitro fertilization of egg. These cells are pluripotent. However they have ethical concerns and can be teratogenic.[2]

Mesenchymal stem cells (MSC) are a group of stem cells which can be derived in adults from bone marrow, dental pulp, adipose tissues or extraembryonic tissues like umbilical cord or placental tissues.[3] Recently, mesenchymal stem cells (MSCs) isolated from various parts of the placenta (PMSCs) are established as a rich, allogeneic, and sustainable source of MSCs in comparison to *bone marrow MSCs (BM-MSCs)*. PMSCs can be banked postnatally for future autologous and allogeneic applications in the treatment of diseases.[4]

PMSCs are employed in the treatment of various diseases including cancer, neurological, bone, and cardiovascular disorders. Developments in cell therapy and opportunities of Cell banking has made this procedure possible. Historically placenta has been used in traditional medicine in China, Japan and certain tribes in India. It was used for treating infertility, weakness, and enhancing reproductive function. Thereafter placental extracts were used as anti aging and for beauty therapy globally. The first use of amniotic membrane was in Ophthalmology in 1910.[5] Placental extracts and tissues and their effect on reproductive system were described in early 20th century. It was the first successful transplantation of cord blood cells in Fanconi anemia which caught the researchers' interest in cord blood stem cells.[6] This article reviews uses of various cells of placenta for treatment especially mesenchymal stem cells and current evidence for their usage in clinical practice and a comment on newer research frontiers.

Postpartum placenta is a disc of 16-20 cms in diameter weighing approxiamately 500 gms. The main cell types of placenta are trophoblasts, mesenchymal cells, endothelial cells. The fetal surface has chorion and amniotic membrane with umbilical cord entering it. Amniotic membrane is thin, transparent, is made of single layered epithelium and amniotic mesenchymal cells. Chorionic membrane is made up of fibroblasts and huge numbers of trophoblast cells. The various components of placenta used for clinical usage are cord blood cells and cord blood serum, various types of differentiated cells, placental extracts and lyophilizates, amniotic and chorionic membrane patches and at times entire placental tissue fragments.[7] Such substances have been used in original form as well as after processing and sublimation. These tissues have to undergo sterilization and decellularisation before being used. Various protocols have been devised for these processes. The variability in the mode of extraction can alter the final composition and growth factor concentration.[8] Methods of application widely vary such as subcutaneous, intramuscular, intravenous, or oral administration.[9]

USAGE OF PLACENTAL CELLS

Trophoblasts cells have a reduced expression of major histocompatibility complexes (HLA-A, HLA-B, and HLA-C), and apoptosis inducing mechanisms and thus are not rejected by the maternal immune system. Other placental cells also have minimal expression.[10] Trophoblasts cells produce hormones like estradiol, progesterones and

chorionic gonadotropin for inducing pregnancy changes in mother and development of fetus. They enhance reproductive and immune functions and are used for similar actions therapeutically. These cells do get transported in to maternal circulation and can remain viable there for few days. Now isolation of fetal cells from maternal circulation is used for mainly diagnosing hereditary disease and also preeclampsia.

CORD BLOOD CELLS

Umbilical cord blood is an easily accessible alternative to the bone marrow as a source of hematopoietic stem cells, useful for haematological and metabolic pathologies.[11] Because of HLA matched donor pooling, cord blood RBC s can be used for the intrauterine blood transfusions in premature babies.

PLACENTAL EXTRACT

Post full-term delivery human placental tissues can be lysed to obtain placental extract. It contains a wide range of proteins, minerals, amino acids, and steroid hormones.[12] They have been used for wound healing, anti inflammatory actions widely. The extracts have been used in ulcers, postoperative wounds and burn wounds. By increasing TGF-â in the early phase and VEGF in the late phase of regeneration, along with increase of FG, CD31 expression, and amplification of angiogenesis, placental extract has ability to cause wound healing.[13] Widely they have been used to enhance reproductive and fertility issues using their hormonal advantages. They decrease the inflammatory cytokines like tumor necrosis factor and IL-6 and IL-1. In animal experiments they have been used for treatment of chronic fatigue, behaviour problems and menopausal symptoms of vaginal atrophy also.

ISOLATED PLACENTAL CELLS

MSCs from extra-embryonic tissues such as the placenta express ESC specific markers including Nanog homeobox protein, octamer- binding transcription factor, Tra-1-60, Tra-1-81, stage specific embryonic antigen-3, and stage specific embryonic antigen-4 which are critical pluripotent markers that maintains cell's "stemness" or ability to remain an undifferentiated state.[14]

PMSCs from fetal origin (from chorionic plate, amniotic membrane, umbilical cord) may have a superior advantage in terms of therapeutic applications in comparison to PMSCs from maternal origin. (decidual parietalis). PMSCs have tri-lineage differentiation abilities to form adipocytes, chondrocytes, and osteoblasts. MSC based therapies have been utilized in various disease models associated with tissue damage, inflammation and have led *to successful tissue repair and regeneration*.[15] There is accumulative evidence suggesting that PMSCs can be exploited as therapeutic tools for the treatment of cancer.[16]

Completed clinical trial studies employing the use of MSCs derived from various parts of the placenta for the treatment of diseases (Table 1).[17,18]

SIDE EFFECTS

A recent meta-analysis study from 62 randomized clinical trials reported nine serious adverse events post MSC treatment which included death, infection, diarrhea, central nervous system disorders, arrhythmia, urticaria/dermatitis, vascular disorders, fever, and localized injection site adverse events. Nonetheless, MSC administration was not correlated to these serious adverse events not directly nor significantly due to its low odds ratio value in all above mentioned events except for transient fever.[19]

STORAGE AND BIOBANKING

Appropriate storage and long term biobanking is essential for usage and research. Cryopreservation is apt for placenta and its tissues Cord blood serum, placental extracts, cell suspensions, chorionic and amniotic membranes, and placental tissue are all suitable for cryopreservation procedures.[20]

Table 1: Clinical trial studies employing use of MSC's

CT02644447	UC- MSCs	Premature ovarian failure (POF)	1/2	10×10^6 MSCs were injected into the ovary of patients under transvaginal ultrasonographic (TVUS)-guidance MSCs were implanted with (8 sub.) or without collagen (6 subj.) scaffolds to the ovaries of POF patients.	MSCs treatment restored overall ovarian function as demonstrated by increased estradiol concentrations, improved follicular development, and increased in antral follicles in 6/14 subjects. Importantly, 2/14 subjects conceived naturally in women with POF after treatment.[17]
T02313415	UC- MSCs	Uterine infertility	1	1×10^7 MSCs loaded into collagen scaffold were implanted into the uterine cavity following an adhesion separation procedure. Endometrial proliferation and differentiation were assessed after therapy.	Improvement in endometrial proliferation, differentiation, and neovascularization following treatment. After 3 years, 10 out of 26 patients had become pregnant, and eight of them had delivered live babies with no obvious birth defects and without placental complications.[18]

CONCLUSION

Whilst the utilization of PMSCs for therapeutic application has garnered interest with growing number of studies, clinical employment of PMSCs is still in nascent stage. It is clear that long term studies are required to thoroughly evaluate any adverse effects associated with PMSC therapy.

KEY POINTS

1. Placenta is a clinically relevant source of tissue for the manufacture of allogeneic MSCs for the treatment of many patients.
2. Most of the works on MSCs are fundamental and experimental. A systematized MSC isolation technique needs to be adopted for large scale expansion in clinical trial studies to avoid ambiguity in results acquired.
3. MSC based therapies have been utilized in various disease models associated with tissue damage, inflammation and have led to successful tissue repair and regeneration.

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Review of Technology Use in Fetal Medicine

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INTRODUCTION

Fetal Medicine has emerged as a specialty focussing on the health and wellbeing of the unborn fetus. Contemporary advancements in this area have resulted in routine use of sophisticated antenatal sonographic screening and techniques including prenatal genetic diagnosis and fetal surgery. Most fetal treatment methods necessitate accessing the fetus *in utero*, and non-invasive procedures have been a part of pregnancy care for a long time. In recent years, the field of fetal medicine has witnessed a remarkable rejuvenation, thanks to rapid advancements in technology. The aim of this article is to explore the transformative impact of cutting-edge technologies on fetal medicine, highlighting how these innovations are reshaping prenatal care and improving outcomes for both mothers and babies.

HIGH RESOLUTION/ MULTIDIMENSIONAL ULTRASOUND IMAGING

The history of medical ultrasound reveals that "echo technology" was used in different disciplines including the military and gradually got adapted into the field of diagnostic medicine in the mid part of the twentieth century[1]. Present day ultrasound machines have improved imaging with excellent grey scale clarity and enhanced "far field" resolution. This has led to greater diagnostic potential while screening for fetal structural anomalies and even a gradual "preponement" of the fetal anatomy scans. More than 80% of fetal anomalies are detected in first trimester nowdays. Modern fetal medicine relies heavily on sophisticated imaging technologies. High-resolution ultrasound, 3D/4D imaging, and magnetic resonance imaging (MRI) have revolutionized the way healthcare professionals visualize and diagnose fetal conditions. These advancements provide detailed insights into the developing fetus, enabling early detection and intervention for potential issues. Fig. 1 shows the enhancement of contour lines by "silhouette" imaging while Fig. 2 depicts surface rendering of a 3D image of fetus in first trimester. With technical improvements and the

Fig. 1: "silhouette" mode

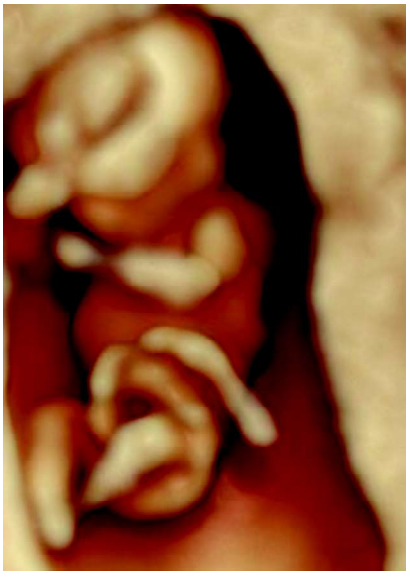

Fig. 2: 3D surface rendering

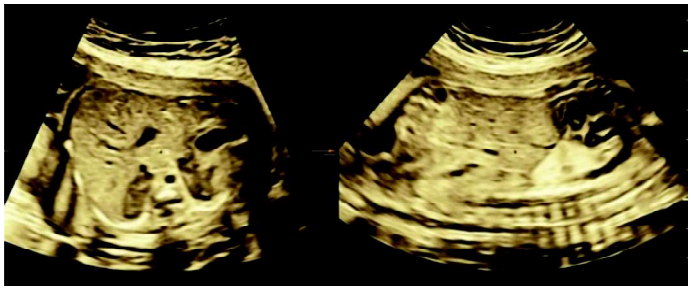

Fig. 3: Biplane imaging

development of different multiplanar display modes, simplified rendering options and easier operation modules, it was possible to get quicker image rendering due to accelerated processing power of the new age computers. Recent years have seen significant improvement in image quality and multiplanar imaging has been a valuable addition to the conventional imaging methods[2]. Fig. 3 shows "biplane"imaging where even in a 2D set up one can simultaneously evaluate the fetus in 2 separate planes in real time. Use of such technology helps in structural evaluation leading to detecting and prognosticating fetal anomalies.

NEW AGE FETAL GENOMIC MEDICINE

Molecular Genetics has redefined the way we understand diseases and genomic medicine is a new buzz word. The integration of genomics into Fetal medicine has opened new frontiers for prenatal diagnosis which allows logical care for potentially untreatable conditions. Genetic counseling based on genomic information empowers parents with valuable insights into potential risks and enables personalized care plans. While the past few decades were witness to increased use of prenatal sampling by amniocentesis for fetal karyotyping, the recent trend has made use of *cytogenetic chromosomal microarray (CMA)* (Fig. 4). Analysis of the chromosomal microarray is performed either by arrays like comparative genomic hybridization or by using a *single nucleotide polymorphism (SNP)*. This technology is considered comparable to traditional karyotyping for detecting of major chromosomal imbalances such as abnormalities in number (aneuploidies), major deletions/duplications or rearrangements like unbalanced translocations but it also offers an additional diagnostic benefits by revealing sub-microscopic imbalances or copy number variations that are too small to be seen on a standard G-banded chromosome preparation. These small or submicroscopic imbalances are also referred to as microdeletions and microduplications. These changes are of clinical significance when they involve specific genomic regions that can be the cause of sequelae. It may also be possible that some microdeletions/duplications may remain asymptomatic and not be associated with adverse clinical phenotypes. Microarrays generally add more information than traditional karyotyping in cases that are associated with a spectrum of clinical phenotypes that may range from benign to severe, while in some situations, the clinical significance may simply be unknown. These "variations of uncertain significance" can pose a challenge for prenatal diagnosis and prognostication of the findings. In such cases genetic counseling prior to prenatal CMA greatly facilitates delivery of complex results. In prenatal diagnostic samples with a normal karyotype, chromosomal microarray will diagnose a clinically significant subchromosomal deletion or duplication in approximately 1% of structurally normal pregnancies and 6% with a structural anomaly [3]. Hence in cases of fetal anomalies it has become an accepted policy to offer CMA instead of only karyotyping. Pre-test counseling is useful as a method to increase awareness of the parents who accept the genetic tests. It would be a good clinical practice point to offer detailed pre-test information to highlight the primary differences between the benefits, limitations and diagnostic scope of CMA versus the powerful but limited screening nature of non-invasive prenatal diagnosis using cell-free fetal DNA. When we discuss new technology, it is not just about the technique themselves but also a new approach in clinical medicine to assimilate these techniques into daily practice.

Fig. 4: Cytogenetic microarray

Next generation sequencing has made it possible to arrive at precise genetic diagnoses at the molecular level and facilitated prediction of risk of recurrence based on the primary condition. In addition to nuclear genetics, mitochondrial DNA sampling is also now possible and available. The use of whole exome sequencing has definitely increased the answers to erstwhile "unexplained" conditions but it has also raised several challenges in interpretation and there is a lot of caution to be exercised in implementing this practice in prenatal medicine [4].

The use of *Non-invasive prenatal testing (NIPT)* allows for the effective screening for chromosomal abnormalities with a simple blood test, reducing the need for invasive procedures. This test is now also used for detecting fetal Rhesus status in cases of rhesus negative mothers. This helps in planning special care for fetuses at risk of anemia due to maternal isoimmunosation.

Newer techniques of genetics are developing at a rapid pace.It has become necessary for all present day practitioners in Fetal medicine to keep abreast the changing paradigms of genetic testing and interpretations. Infact this surge of technology has led to establishment of multidisciplinary teams for care in Fetal Medicine.

TECHNOLOGY IN OPEN AND MINIMALLY INVASIVE FETAL SURGERY

Technological advancements have also impacted fetal surgery, offering less invasive and more precise techniques. In-utero interventions for conditions like spina bifida and congenital heart defects have shown promising outcomes, demonstrating the potential for early intervention to improve long-term health outcomes. The goal of fetal surgery is to improve the outcome for the baby by addressing issues before birth. There are different types of fetal surgery, and the specific approach depends on the nature of the fetal condition. The "Harrison's principles for fetal intervention" define certain conditions as ideal for the planning and execution of fetal surgery like repairing spina bifida, correcting heart defects, or addressing urinary tract obstructions. These conditions have a known natural course and no available postnatal treatment

Fetoscopic surgery again provides a minimally invasive route to address problems like unbalanced placental anastomoses in twin to twin transfusion syndrome (TTTS). The natural history of (untreated) TTTS was known to be associated with perinatal death in 90% of cases and neurological impairment in 50% of survivors. The superficial placental anastomoses in monochorionic pregnancies treated with *fetoscopic laser ablation (FLA)* of has been considered the standard of care for severe TTTS, with most groups reporting survival of at least one twin in 80–90% of cases and a 3–5% rate of neurological impairment among survivors after prenatal treatment [5].

In utero Spina bifida repair was evaluated in the MOMS trial[6] in the USA and has established a definite benefit of intervention versus expectant management by a reduction in the need for shunts postnatally in the cohort that had in utero repair. Such surgeries are marvels of human endeavor coupled with technology like fetal anesthesia, miniature instruments with unique techniques of repair of both fetal and maternal tissues.

While the emerging technology and its obvious advantages are huge motivators for many practitioners, fetal surgery must be undertaken only after careful weighing of the risk versus benefit ratio and in the spirit of *primum non nocere*.

EMERGING TECHNOLOGY OF THE INNOVATIVE FETAL MONITORING DEVICES

Monitoring the fetal heart rate and patterns has been a method of establishing fetal wellbeing. Continuous monitoring of fetal heart rate, movement, and other vital parameters allows for real-time assessment, providing healthcare professionals with valuable data to ensure the well-being of both mother and the fetus in utero . New technology allows wearable devices and remote monitoring technologies that have become integral components of fetal medicine. A variety of CFM devices have been developed, however no specific approach or design appears to be advantageous due to high levels of inter-device and intra-device variability [7]and this field is still looking for final answers.

USE OF TELEMEDICINE IN PRENATAL CONSULTATIONS

Telemedicine is a new concept of making clinical consultations available at remote sites through new technology. The advantages of this development in technology is that it transfers expert opinions of specialists in several specialties and in varying degrees of complexity from far-off geographical locations. These doctors therefore can provide advice and share care of patients practically anywhere if internet connectivity is possible. The widespread adoption of telemedicine has facilitated remote prenatal consultations, making healthcare more accessible for expecting mothers, especially those in remote or underserved areas. *Virtual appointments* enhance the efficiency of communication between healthcare providers and patients, ensuring timely guidance and support throughout the pregnancy journey. Telemedicine may be able to reduce the demand for care and inequality in access [8] . The use of telemedicine to co-ordinate with a multidisciplinary team of experts in Fetal Medicine can facilitate the patient's contact with professionals specialized in high-risk prenatal care and overcome the administrative hurdles in many cases. One of the fallouts of the Covid-19 pandemic was to allow this field of telemedicine to emerge as a marvel of technology and understanding its applications, this technology is here to stay.

BIG DATA AND ARTIFICIAL INTELLIGENCE (AI)

Artificial Intelligence (AI) is the new buzzword in the modern technological era. The advent of language models, powered by natural language processing and pretrained language models, have demonstrated excellent effectiveness in text generation as well as understanding. Artificial intelligence (AI), defined as the ability of computers to perceive, process, and utilize large quantities of information, has permeated

every sector of the economy and is beginning to manifest changes in clinical work [9]. These models are able to assist Fetal Medicine doctors by aiding in decision-making processes, and allowing simultaneous discussion of condition between doctors and patients.

The integration of AI language models in Fetal Medicine faces limitations and challenges based on ethical considerations, privacy concerns, and the potential for algorithmic biases. Rigorous validation studies are required to evaluate transperancy of AI models. It is essential to maintain a patient-centered approach and to mitigate the risk of overreliance on AI systems.The potential benefits and precautions associated with the utilization of AI language models in the context of Fetal Medicine includes the analysis of vast datasets through AI applications for more accurate risk assessments and predictive modeling. The machine learning algorithms aid in identifying patterns and trends, assisting healthcare providers in making informed decisions and improving diagnostic accuracy.

CONCLUSION

The "rejuvenation" of use of technology in fetal medicine is ushering in a new era of prenatal care, characterized by enhanced diagnostic capabilities, personalized treatment plans, and improved accessibility. Fetal imaging has touched new heights and diagnostic genomics have opened new frontiers while fetal "therapy" brings in hope for correcting nature's maladies.

KEY POINTS

1. High-resolution ultrasound, 3D/4D imaging, and magnetic resonance imaging (MRI) provide detailed insights into the developing fetus, enabling early detection and intervention for potential issues
2. Newer technologies like cytogenetic chromosomal microarray (CMA) offer additional diagnostic benefits by revealing sub-microscopic imbalances or copy number variations
3. As technology continues to evolve, the synergy between medical expertise and cutting-edge tools and intervention like fetoscopic surgery promises a brighter future for the well-being of both expectant mothers and their unborn children.

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PROCEEDINGS OF AOGD CLINICAL MEETING
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CASE REPORT

Hematuria—An Unusual Presentation of Placenta Accreta Spectrum

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ABSTRACT

Bladder bleeding in cases with the placenta percreta spectrum is a rare clinical presentation and lacks a standard management strategy. We present a case of a 31-year-old, G3P1L1A1 at 28+5 (U) with previous LSCS with pre-term premature rupture of membranes with anhydramnios with placenta accreta spectrum (PAS). She was an unbooked case and presented to our gynae-emergency with complaints of leaking per vaginum for two months and bleeding per vaginum for 2 days not associated with pain lower abdomen. She was kept on conservative management initially with strict antepartum hemorrhage and chorioamnionitis charting from Day 1-3. On day 4, the patient started complaining of hematuria and an MRI pelvis was done which was suggestive of placenta accreta spectrum. She was taken up for classical cesarean followed by hysterectomy with informed consent, arranging adequate blood products, and informing a multidisciplinary team. Her intraoperative findings were as follows: a cystic structure of 15×15 cm was seen adjacent to the lower uterine segment which also showed a bulge and increased vascularity. Considering, it to be a distended bladder, we recatherised her, but the size of the mass didn't decrease. We did a classical cesarean followed by a hysterectomy taking care of the cystic structure. Surgeons were called in and the cystic structure was identified as bladder hematoma. Initially, three trials of periurethral suctioning of the bladder were attempted, but it failed. Thereafter, the urinary bladder was incised on its anterior lower aspects, and around 1 liter of clots were extracted. A 3×3 cm hyperemic area was identified on the posterior wall of the bladder with no obvious source of bleeding. 18 G transurethral Foley's catheter was then inserted and the bladder was sutured in two layers. She had an uneventful post-operative period with the removal of the catheter on day 15.

Keywords: placenta accreta spectrum, bladder hematoma, hematuria

INTRODUCTION

Placenta percreta spectrum causing bladder bleeding during the antenatal period poses a great threat to the mother as well as the fetus. It is a rare clinical presentation and lacks a standard management strategy.

CASE REPORT

We present a case of an unbooked patient, 31-year-old, G3P1L1A1 at 28+5 (U) with previous 1 LSCS and one spontaneous abortion followed by dilatation and curettage with leaking per vaginum since 2 months and spotting per vaginum since two days not associated with pain in the abdomen. Her ultrasound revealed appropriate for gestational age fetus with absent liquor and placenta previa. lower part of the uterus with multiple tortuous vessels on its

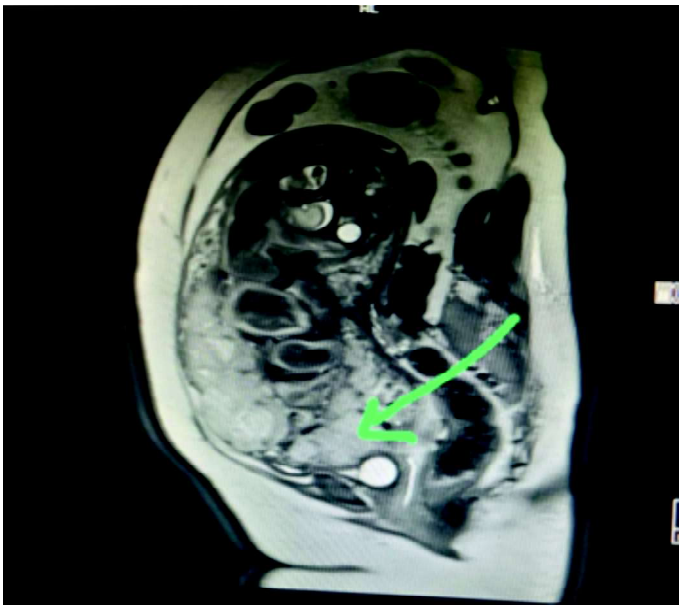

Fig. 1: MRI suggestive of placenta percreta (green arrow)

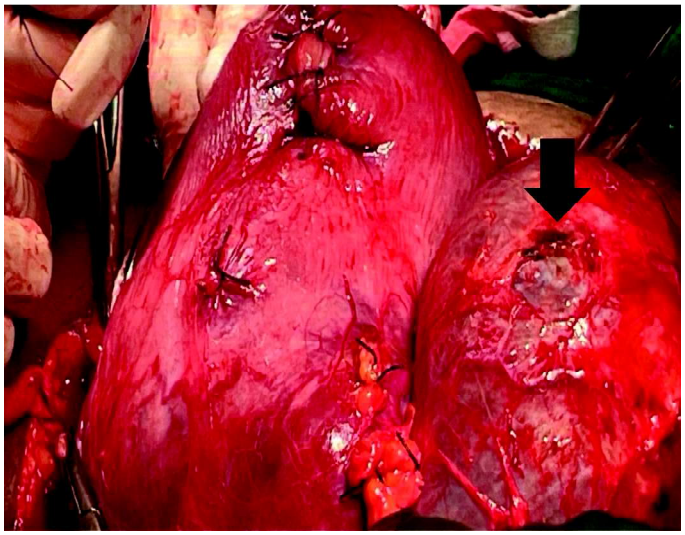

Fig. 2: Cystic structure of 15x15 cm adjacent to lower part of the uterus with tortuous blood vessels overlying it.

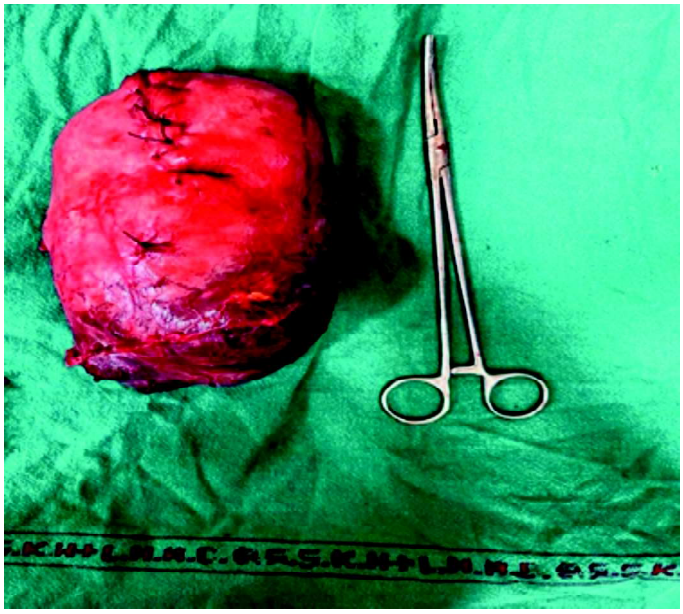

Fig. 3: Hysterectomy specimen

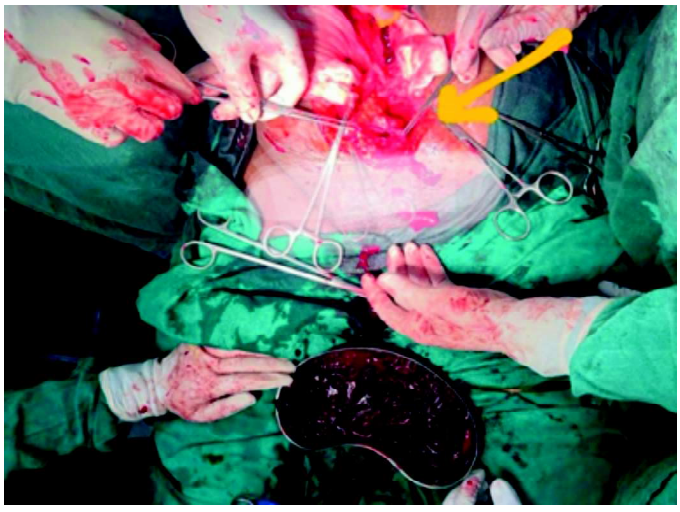

Fig. 4: Cystostomy done and 1 litre of clots removed via the bladder

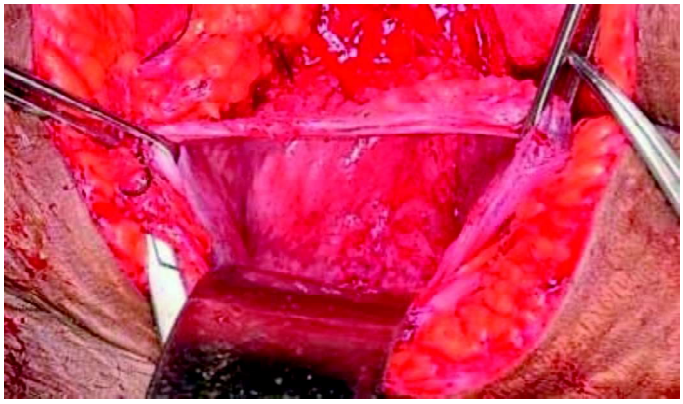

Fig. 5: Hyperemic area seen on posterior wall of bladder

surface (Fig. 2). Considering, it to be a distended bladder, we recatherised her, but the size of the mass didn't decrease. The other possibility was a distended lower uterine segment. We did a classical cesarean followed by a hysterectomy meticulously taking care of the cystic structure (Fig. 3). Surgeons joined in after the hysterectomy and the cystic structure was identified as bladder hematoma. Initially, three trials of periurethral suctioning of the bladder were attempted, but it failed. Thereafter, the urinary bladder was incised on its anterior, and around 1 liter of clots were extracted, Fig. 4. A 3×3 cm hyperemic area was identified on the posterior wall of the bladder with no obvious source of bleeding, Fig. 5. An 18 G transurethral Foley's catheter was then inserted and the bladder was sutured in two layers. She had an uneventful post-operative period with the removal of the catheter on day 15. The histopathology of the specimen retrieved revealed placenta increta.

DISCUSSION

The two main reasons for bladder bleeding are either related to placental invasion or unrelated to it. Placenta-related causes are due to placental villi penetrating the anterior surface of the uterus through the full thickness of the wall of the bladder.[1] The normal smooth muscle tissue for protection is not seen in villi, therefore it can cause bladder bleeding. The dense adhesions post-cesarean section lead to placental villi penetrating through the serosal layer of the uterus into the bladder. The other possible reason for bladder bleeding is the proliferation of tortuous and disordered vessels involving the upper, middle, and lower vesical artery on one or both sides from the posterior and bottom walls of the bladder along with the opening of anastomotic channels. Such vessels are characterized by high output and low resistance and have rapid bleeding when ruptured.[2] Also the friction between the balloon of Foley's catheter and the edematous and congested mucosa of the bladder can be the reason for the rupture of abnormal hyperplastic blood vessels. Treatment for PAS with concomitant bladder bleeding before delivery is termination of pregnancy.[3,4] Treatment of bladder bleeding after delivery is interventional embolization, electrocoagulation hemostasis under cystoscopy, feasible only in cases with mild bladder bleeding while exploratory

laparotomy is the treatment modality in patients of excessive hemorrhage, unstable vital signs and failed interventional embolization.[1]

CONCLUSION

Such cases should be managed in a tertiary-level center. The Presence of experienced obstetricians and the availability of multidisciplinary team members can help provide optimal management in such onerous cases.

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ABSTRACT 1

Enlarged Multicystic Ovaries in An Infertile Woman: Thinking Beyond Controlled Ovarian Stimulation

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INTRODUCTION

Functional Gonadotroph Adenoma (FGA) is a rare, slow-growing pituitary tumor that presents in the reproductive age group with abnormal uterine bleeding, infertility, and Ovarian Hyperstimulation Syndrome. We present the case of a young twenty five year old woman who presented in the endocrinology clinic with complaints of abnormal uterine bleeding and infertility.

ABSTRACT

Our patient was a 25 year old nulligravida and her chief complaints were inability to conceive and abnormal uterine bleeding. She had prolonged cycles of 35-90 days with a heavy flow for 5-30 days for last one and a half years. She was married for two years, there was no other significant history. She was overweight, her BMI being 26.17kg/m2). The examination was unremarkable except for fullness in the lower abdomen. She had a pelvic ultrasound done which showed thickened endometrium (15mm) with enlarged bilateral cystic ovaries (volume 207cc and 227cc on each side). There was no history of ovarian stimulation. Follicular phase hormonal profile showed elevated FSH (14.7 IU/L), suppressed LH (0.216 IU/L), raised E2 (1552pg/ml) along with normal TSH (3.42 m IU/ml), and slightly increased prolactin levels (44.9ng/ml). She was started on Cabergoline and advised a postmenstrual USG. Theca lutein cyst was also ruled out with negative serum beta hCG. As the cystic ovaries persisted in the postmenstrual phase as well, along with similar trends of the hormonal profile, she was given COCs for three months. Still, after three months, the ovaries were enlarged and multicystic (ET 17mm, Right ovary 10.6cm x4.7cm, Left ovary 7.3cm x3.5cm), FSH -18.6IU/L, LH-0.38 IU/L, E2-461pg/ml, we advised an MRI Brain. MRI Brain revealed heterogeneously enhancing suprasellar mass 15x23x23mm suggestive of pituitary macroadenoma. Growth Hormone, ACTH and cortisol levels were within normal limits. There was no defect in Visual field perimetry. She underwent Microscopic Transnasal Transphenoid surgery for pituitary adenoma. The postoperative period was uneventful. Histopathology revealed a Pituitary adenoma. On Immuno-histochemistry: Negative for GH, PRL, ACTH, and TSH; positive for FSH, and LH. Six months postoperatively, she had resumed regular menstrual cycles. Pelvic imaging showed normal-sized bilateral ovaries with ET 8mm. Hormonal profile was also within normal limits (FSH- 7.5IU/L, LH 1.49 IU/L, E2 48pg/ml). She was advised natural contact for six months. She conceived spontaneously and delivered a healthy Girl child weighing 2.52kg.

The final diagnosis was Primary Infertility with Abnormal Uterine Bleeding with Functional Gonadotroph Adenoma (FGA).

Gonadotroph adenomas account for approximately 40% of all pituitary adenomas. They stain positive for FSH, LH, steroidogenesis factor (SF-1), and estrogen receptor-alpha (ERá) on Immunohistochemistry. The majority of immunohistochemically confirmed gonadotroph adenomas are hormonally silent (presenting only with mass effects). However, clinically FGAs are very rare. In premenopausal women, they may present with AUB, infertility, mass effects, or OHSS. Biochemical findings include Hyperestrogenism (increased E2), Serum FSH (normal/ increased), and serum LH (Normal/ low). Pelvic imaging shows multi-septate cysts of variable size in B/L ovaries(anechoic). In postmenopausal women, presentation is similar to that of a nonfunctioning adenoma as the ovaries do not respond to increased FSH. Gonadotropin increase is secondary to menopause. The discrepancy of FSH and LH or FSH'!, LH "!/N may indicate gonadotroph adenoma. Differential diagnosis includes PCOS, OHSS, and granulose cell tumors. Surgery is the mainstay of therapy with an inconsistent role in medical management.

This case was presented to highlight the importance of a rare diagnosis in a woman with usual complaints of AUB and infertility. FGA should be kept as a differential diagnosis in woman presenting with AUB and bilateral cystic ovaries. Elevated FSH with Elevated E2 levels must prompt a search for FGA in a premenopausal woman. Elevated FSH, low/ normal LH, and high/normal E2 in perimenopausal ladies may indicate FGA.

ABSTRACT 2

Rare Presentation of Cesarean Scar Complication: Addition to Diagnostic Dilemmas

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INTRODUCTION

Increasing cesarean section rates have led to a wide range of complications such as cesarean scar pregnancy, and placenta accreta spectrum and the sequelae associated with such surgeries are also inevitable. We present an interesting case of rare presentation of cesarean scar complication adding to our diagnostic dilemmas.

ABSTRACT

25-year-old P2l1A1 with one prior stillbirth and previous cesarean section, presented with irregular bleeding per vaginum off and on for the last 10 months in July 2022. The irregular bleeding was preceded by a medical abortion of six weeks amenorrhoea. It was associated with dull pain lower abdomen. It was medically managed by tranexamic acid and oral contraceptive pills at other facilities. However, the patient was not relieved.

A Diagnostic hysterolaproscopy performed in an outside centre for evaluation of the same revealed as per referral letter: omentum adherent to anterior abdominal wall, bulky uterus, and anterior surface of uterus adherent to bladder with sprouting bluish color growth at the previous scar site. Right ovary visualized normal, left ovary obscured by adhesions. On hysteroscopy normal looking cervical cavity, post wall normal, irregular edematous growth with vascularity present on anterior wall. Cystoscopic evaluation bulging seen in trigonal area with increased vascularity. Urine pregnancy test negative with Beta hCG levels in normal range. Any further procedure was abandoned, and she was referred.

Transvaginal ultrasound examination revealed a heterogenous echogenic mass of 3x2 cm arising from the anterior wall of the uterus with no vascularity. This was confirmed by an MRI pelvis showing an altered signal intensity lesion 3 x2.6 cm with foci of calcification in the anterior lower uterine segment at the previous scar site reaching the endometrial cavity causing overlying myometrial thinning and uterine contour bulge with no bladder invasion, no vascularity along with peripheral calcification making a possibility of subserosal fibroid likely or cesarean scar ectopic pregnancy. Beta hCG was negative.

An emergency exploratory laparotomy was performed. Intraoperatively bladder was densely adherent to the previous scar site with a bluish bulge seen at the previous scar. The left side of the scar near the uterine angle was seen to have already given way with tissue seen projecting out. A transverse incision was given at the site of the previous scar and similar-looking tissue was extracted and margins were freshened. Previous incision scar site repaired. The tissue was sent for histopathology.

The histopathology revealed florid giant cells with about 15-20 nuclei with osseous metaplasia and numerous scattered giant cells admixed with fibrin. The immunohistochemistry showed CD68 positivity in Giant cells and Ki67 in the range of 10-12%. CK 18 was performed to exclude trophoblast in the etiology of giant cells which was negative. P63 was negative. The patient has been on regular follow-ups for the last 1 year with the oncology team and the gynecological team. She has been having regular cycles till this write-up with no clinical symptoms and normal ultrasound findings.

Giant cell tumors are rare benign bone tumors, which occur in young adults of 20-40 years of age. They have a high recurrence rate and a potential for aggressive behavior.

To the best of our knowledge, this is the first case to be reported as a giant cell tumor of the cesarean scar. Two cases of GCT-ST in surgical scars are reported. Both tumors were initially regarded as tumors relapses of a leiomyosarcoma of deep soft tissue and a dermal in situ squamous cell carcinoma, respectively.

GCT-ST occurs as a primary soft-tissue neoplasm and is identical clinically and histologically to giant cell tumor of bone. Provided that GCT-ST is treated adequately by complete excision, a benign clinical course is expected because episodes of distant metastasis and tumor-associated death seem to be exceedingly rare. With the background of a rising cesarean section, a giant tumor of scar site adds another dimension to the diagnostic dilemmas. Adequate surgical resection, achieving clear margins, and close clinical follow-up would be useful in preventing recurrence.

Association
of
Obstetricians & Gynaecologists of Delhi

MAY : PREECLAMPSIA AWARENESS MONTH

Recommendations for Aspirin Prophylaxis

	ACOG (2020)	NICE (2019)	ISSHP (2018)	FIGO (2019)
When to offer Aspirin	Presence of any high-risk factor/two moderate-risk factors	Presence of any high-risk factor/two moderate-risk factors	Presence of any high-risk factor; no recommendation in the presence of moderate risk factors	High-risk on the Fetal Medicine Foundation first trimester combined test
Daily dose	81 mg initiated between 12 and 28 weeks, ideally before 16 weeks	75–150 mg from 12 weeks	75–162 mg, ideally before 16 weeks but definitely before 20 weeks	150 mg at night initiated between 11 and 14 weeks (+6 days) gestation
When to cease Aspirin	Continue until delivery	Continue until delivery	No recommendation	Continue until 36 weeks gestation, delivery, or when pre-eclampsia is diagnosed

Clinical Risk Factors to Identify Women at Risk of Pre-eclampsia

RISK FACTORS	ACOG (2020)	NICE (2019)	ISSHP (2018)	FIGO (2019)
CHRONIC HTN	High	High	High	Included
TYPE 1/2 DIABETES	High	High	High	Included
RENAL DISEASE	High	High	High	Included
AUTOIMMUNE DISEASE	High	High	High	Included
HISTORY OF PREECLAMPSIA	High	High	High	Included
MULTIFETAL GESTATION	High	Moderate	High	Included
USE OF ART	Not included	Not included	High	Included
HIGH BMI	Moderate (>30 kg/m²)	Moderate (>35 kg/m²)	High (>30 kg/m²)	Included
NULLIPARITY	Moderate	Moderate	Not included	Included
FAMILY HISTORY OF PREECLAMPSIA	Moderate	Moderate	Not included	Included
PREGNANCY INTERVAL OF >10 YEARS	Moderate	Moderate	Not included	Included
MATERNAL AGE	Moderate (>35 years)	Moderate (>40 years)	Not included	Included
MATERNAL HEIGHT	Not included	Not included	Not included	Included
OBSTETRIC HISTORY (LBW/SGA/PREVIOUS ADVERSE OUTCOME)	Moderate	Moderate	Not included	Included
SOCIODEMOGRAPHY (BLACK/LOW SOCIOECONOMIC STATUS)	Moderate	Not included	Not included	Included

The Lancet, 2021

Journal Scan

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Stillbirth risk and smallness for gestational age according to Hadlock, INTERGROWTH-21st, WHO, and GROW fetal weight standards: analysis by maternal ethnicity and body mass index

Gardosi J, Hugh O. Am J Obstet Gynecol. *2023; 229 (5): 547. e1-547. e13.*

INTRODUCTION

A standardized growth chart is extremely important to monitor fetal growth and timely identify the pregnancies at risk. Stillbirths can be avoided to a large extent by timely detection of small for gestational age fetus. There is an absence of international consensus on the use of a specific growth chart. Hence, it is imperative that clinical practice reflects outcome-based evidence.

OBJECTIVE

This study investigated 4 internationally used fetal weight standards and their accuracy in identifying stillbirth risk in groups of different ethnic and maternal size in a heterogenous population.

STUDY DESIGN

They analysed routinely collected data from more than 2.2 million pregnancies. The customized GROW standard chart which was adjusted for maternal height, weight, parity, and ethnic origin was compared with three population-based fetal weight standards (Hadlock, Intergrowth-21st, and World Health Organization). SGA birthweight and the risk of stillbirth was determined for the two largest ethnic groups in their population (British European and South Asian) , in 5 body mass index categories, and in 4 maternal size groups with normal BMI ranging from 18.5-25.0 kg/m^2.

RESULTS

Stillbirth rates were higher in South Asian pregnancies than British-European pregnancies and increased in both groups with increasing BMI. The rate of SGA was 2 to 3-fold higher for South Asian babies than British European based on the population-average standards (Hadlock: 26.2% vs 12.2%; Intergrowth-21st: 12.1% vs 4.9%; World Health Organization: 32.2% vs 16.0%) , but were same as per the customized GROW standard (14.0% vs 13.6%) . Despite the wide variation, each standard's SGA cases had increased stillbirth risk compared with non-SGA cases. Similar stillbirth risk was found in all standards when the SGA rate was fixed at 10% by varying their respective thresholds for defining small for gestational age. When analyzed across BMI subgroups, the SGA rate according to the GROW standard increased with increasing stillbirth rate, whereas SGA rates according to Hadlock, Intergrowth-21st, and World Health Organization fetal weight standards declined with increasing BMI.

STRENGTHS AND LIMITATIONS

The large, routinely recorded dataset allowing analyses within subgroups of a relatively rare outcome—stillbirth—in pregnancies complicated by SGA in different BMI categories which were further divided into maternal size subgroups in the normal BMI category, and performed in 2 ethnicity cohorts is the strength of this study. A limitation could be that fetal weight standards were assessed using the weight at birth. However, ultrasound imaging is usually done only selectively, based on perceived risk. Moreover, unlike birthweight, the accuracy of fetal weight estimation is reduced by maternal obesity, which would have affected the analysis and reliability of the findings.

CONCLUSION

The comparison between population-average and customized fetal growth charts requires examination of how well they identify pregnancies at risk of adverse outcomes within subgroups of a heterogeneous population. In both ethnic groups studied, increasing maternal BMI was accompanied by increasing stillbirth risk, and this trend was reflected in more pregnancies being identified as SGA only by the customized standard. On the contrary, SGA rates fell according to each population-average standard, thus hiding the increased risk of stillbirth associated with high maternal BMI.

KEY POINTS

- This study compares the ability of 4 fetal weight charts to detect SGA related stillbirth risk in different maternal ethnicity and BMI groups.
- Missed SGA leading to false-negative assessment has added importance because of the challenge of high maternal BMI in antenatal care.
- Population-average and un-customized growth charts hide the association between FGR and stillbirth risk in high BMI pregnancies.
- A customized approach reduces false positive assessment and helps in identification of growth restriction related stillbirth risk in women with high BMI.

Personalized stratification of pregnancy care for small for gestational age neonates from biophysical markers at midgestation

Papastefanou I, Wright D, Syngelaki A, Akolekar R, Nicolaides KH. Am J Obstet Gynecol. *2023;229 (1): 57. e1-57. e14.*

INTRODUCTION

Timely identification of pregnancies at high risk of delivering small for gestational age neonates may improve the management of this condition and help in reduction of the associated adverse perinatal outcomes. In a series of publications, a new competing-risks model for small for gestational age prediction was developed. It was seen that the new approach had a superior performance than the traditional methods. The next step in the appropriate management of small for gestational age is the timely assessment of high-risk pregnancies based on an antenatal stratification plan.

OBJECTIVE

This study was designed to demonstrate the stratification of pregnancy care based on individual patient risk derived from the application of a competing-risk model for small for gestational age combining maternal risk factors along with sonographic estimated fetal weight and uterine artery pulsatality index at midgestation.

STUDY DESIGN

This was a prospective observational study of 96,678 singleton pregnancies undergoing routine ultrasound for the estimation of fetal weight and uterine artery pulsatality index at 19 to 24 weeks. The competing-risks model for SGA was used to create a patient-specific stratification curve capable to define a specific timing for repeat ultrasound after 24 weeks. They examined different stratification plans with the intention to detect approximately 80%, 85%, 90%, and 95% of SGA neonates with birthweight <3rd and <10th percentiles at any gestational age at delivery until 36 weeks of gestation. All pregnancies were offered a routine ultrasound at 36 weeks.

RESULTS

The stratification of pregnancy care for SGA can be based on a patient-specific stratification curve. Risk factors from maternal history, low estimated fetal weight, and increased uterine artery pulsatality index shifts the personalized risk curve on the higher side. The timing of assessment for each pregnancy depends on the degree of shifting of the curve. If the objective of the antenatal plan was to detect 80%, 85%, 90%, and 95% of SGA neonates at any gestation at delivery until 36 weeks, the median (range) proportions (percentages) of population examined per week would be 3.15 (1.9-3.7) , 3.85 (2.7-4.5) , 4.75 (4.0-5.4) , and 6.45 (3.7-8.0) for SGA <3rd percentile and 3.8 (2.5-4.6) , 4.6 (3.6-5.4) , 5.7 (3.8-6.4) , and 7.35 (3.3-9.8) for SGA <10th percentile, respectively.

CONCLUSION

The competing-risks model provides a personalized, continuous and effective risk stratification of pregnancy care for small for gestational age which is based on individual characteristics and biophysical markers measured at the midgestation ultrasound examination.

KEY POINTS

- Early detection of SGA fetus is crucial for providing timely and optimal pregnancy care for the best fetomaternal outcome.
- The competing risk model encompasses maternal factors along with ultrasound estimated fetal weight and uterine artery pulsatality index at the midgestation of pregnancy between 19 to 24 weeks.
- It helps to create a patient-specific stratification curve which can aid in determining a specific time for the repeat ultrasound to be done for the early detection of small for gestation age fetus.
- This method of stratification curve has been found to be superior to that of screening by maternal characteristics and medical history alone.

The efficacy of emergency cervical cerclage in singleton and twin pregnancies: a systematic review with meta-analysis

Hulshoff CC, Bosgraaf RP, Spaanderman MEA, Inthout J, Scholten RR, Van Drongelen J. Am J Obstet Gynecol MFM. *2023;5 (7): 100971.*

INTRODUCTION

An emergency or rescue cerclage can be offered to women presenting with dilatation and prolapsed membranes in the second trimester of pregnancy due to cervical insufficiency. This study aimed to investigate the effectiveness of emergency cerclage in singleton as well as twin pregnancies in the prevention of extreme premature birth.

DATA SOURCES

A systematic literature search was performed in PubMed and Embase from the time of inception till June, 2022 with respect to transvaginal emergency cerclages.

STUDY ELIGIBILITY CRITERIA

All studies who had atleast 5 patients and reported survival after transvaginal, cervical emergency cerclages were included.

METHODS

An adjusted Quality In Prognosis Studies tool was used to assess the quality and risk of bias in the included studies. In addition, random-effects meta-analyses and meta-regressions were performed for the primary outcome, which was survival.

RESULTS

The literature search yielded 96 studies, comprising of 3239 women, including 14 studies with an expectant management control group, comprising of 746 women. Emergency cerclage was associated with an overall survival of 74%, fetal survival of 88% and neonatal survival of 90%. Similar survival was seen in both the singleton and twin pregnancies, with a pregnancy prolongation of 52 and 37 days and gestational age at delivery of 30 and 28 weeks, respectively. A significant inverse association was seen between the mean gestational age at diagnosis and pregnancy prolongation as per the Meta- regression analysis. There was no association between gestational age at diagnosis or dilatation and the gestational age at delivery. Compared to expectant management, emergency cerclage showed significantly increased overall survival at the rate of 43%, fetal survival by 17% and neonatal survival by 22%. Pregnancy prolongation of 37 days and a 55% reduction in delivery at <28 weeks was also seen. These effects were seen more profoundly in singleton pregnancies as compared to twin pregnancies.

STRENGTHS AND LIMITATIONS

The main strength of this review is that it combines the results of a large number of small studies. Moreover, included pregnancies were divided into different groups for sub analyses, which reduces the effect of confounders. The limitation of this study is that most of the included studies had retrospective observational design and not prospective randomized control designs leading to selection and publication bias. Moreover, due to the non-standardized treatment protocols and outcome measures, the results suffer from clinical and methodological heterogeneity.

CONCLUSION

Emergency cerclage in pregnancies threatened by extreme premature birth due to cervical insufficiency is associated with significantly higher survival, pregnancy prolongation and reduction in delivery at <28 weeks of gestation, compared to expectant management. Survival rate was similar in singleton as well as twin pregnancies, implying that emergency cerclage should be considered in both.

KEY POINTS

- This systematic review aims to assess the outcome of emergency cerclage in both singleton and twin pregnancies and compare it with expectant management.
- It has included all reported studies on emergency cerclages with >=5 participants and concluded that placement of encirclage significantly improves survival rate and leads to prolongation of pregnancy in both singleton as well as twins.
- The mean gestational age at delivery is 30 weeks, independent of dilatation and gestational age at diagnosis, after the placement of cerclage.
- This study provided relevant data which can be used in the counselling of couples.

News Flash

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HYSTERECTOMY: JUSTIFYING INDICATIONS & NUMBERS

Unless you've been living under the rock, its hard to miss the raking debate over the necessity versus futility of the most common gynecological procedure being performed world-wide. Yes, you've guessed it right: Hysterectomy! (Hindustan Times April 2, 2024; The New York Times, March 24, 2024; March 9, 2024 Economic & Political Weekly)

Quoting data from the fifth National Family Health Survey, (NFHS 5), 2019-21, 3% of women between ages 15-49 underwent hysterectomy. So far, so good! But the catch lies in the fact that the median age in this group is 34.6 years. Just to keep things in statistical perspective, the median is the most frequently appearing number in that group. If education really has something to do with it, 7.1% of these women have never received any schooling. The prevalence of this procedure in rural areas is 3 times that of urban areas.

Now let us take a similar look at some international data to see how we compare and contrast. As per the National Center for Health Statistics, National Health Interview Survey, 2021, in United states, age adjusted data suggests that Asian non-Hispanic women are those least likely to undergo a hysterectomy. Rates of this extirpative procedure indeed are inversely proportional to women's level of education, to her level of urbanization, and to the family's income and all of these differences are statistically significant. More importantly, the data for age is conveniently grouped as 18-44 years and others, so that any break up under 40 years is conspicuous by absence. However, 18-44 group constitutes only 2.2% of the total number of women undergoing hysterectomy. A similar picture emerges from Canada as well where hysterectomies for benign indications have increased over the last decade.

A more pragmatic approach draws attention to the recent meta-analysis (A Systematic Review and Meta-analysis. Obstetrics & Gynecology 141(1):p 35-48, January 2023.) of

emergency peripartum hysterectomy published in IJOG, 2023, (which incidentally also cites the author's own series of 56 cases). Undeniably, the growing numbers of peripartum hysterectomies would contribute to the total number of hysterectomies under 40.

The governmental initiative of recording all hysterectomies under 40 years is a welcome step in this direction. FOGSI has also through its '*Preserve the uterus campaign*' expressed solidarity with the cause of reducing numbers of unindicated hysterectomies. Until we get more data on under 40 hysterectomies let's try reducing under 40 hysterectomies with all the available medical approaches. As data suggests, addressing social factors such as enhancing women education, awareness and financial standing could also help us reduce these numbers while concomitantly making our world a better place to live in.

AGAINST MALICE AGAINST GYNECOLOGISTS

Dr Nitya Anand, the man who developed, the only non-hormonal non-steroidal contraceptive pill of the world, Centchroman, which occupies a place of pride in the Family Planning Program of India since 2016. Developed indigenously by the Central drug research institute, Pune, it is the proverbial feather in the cap of Indian medical research in the international arena.

Dr Nitya Anand, the man behind this success story breathed his last at the SGPGI Lucknow on January 27, 2024, at the age of 99. He served the CDRI, firstly, as a gifted scientist, then as the chair of the division of Medicinal Chemistry, for a nearly a decade, from 1963 onwards, and later as Director for another decade thereafter. Dr Anand, a Padma Shree awardee, has to his credit more than 400 research papers and over 130 patents.

Centchroman, pharmacologically Ormeloxifene, belongs to the category of selective estrogen receptor modulators (SERMs). An anti-implantation agent, it is anti-estrogenic at the uterine receptors without adversely affecting estrogen influence in other parts of the body. It is devoid of any troublesome gastro-intestinal side effects or break through bleeding. Rebound fertility is not a concern and the offsprings born to mothers experiencing failure have been followed up to confirm normal milestones. With no effect on lactation, it can be an effective contraceptive choice in the peripartum period.

Snitch Snatchers

Dr. Preeti Sainia
CMO NFSG
Department of Obstetrics and Gynaecology, ABVIMS & RML Hospital

1. Incidence of major anomalies in Fetus ina diabetic mother with hba1c 13% is
   A. 20% B. 10%
   C. 15% D. 25%
2. Risk of chromosomal anomaly in the fetus in 2nd trimester ina woman age 40 yrs
   A. 1 in 1250 B. 1 in 714
   C. 1 in 294 D. 1 in 86
3. Risk for recurrence of ntds with 2 affected siblings
   A. 10% B. 2-4%
   C. 15% D. 25%
4. An intrauterine growth restricted fetushas oligomanios and an abnormal calvarium. Which antihypertensive mayhave caused it
   A. Verapamil B. Methyldopa
   C. Lisinopril D. Nifedipine
5. Which of the following pregnancy outcomes are assosiated with maternal subclinical hypothyroidism
   A. Preeclampsia B. Atillbirth
   C. Placenta Previa D. PPH
6. Which is a risk factor for puppp
   A. African American Ethinicity B. Multifetal gestation
   C. Female Ffetus D. Nulliparity
7. Superfecundation results from
   A. Fertilization of 2 ova in the same cycle B. Fertilization of 2 ova in 2 different cycles
   C. Single coitus D. Coitus during the course of normal pregnancy
8. A female is given i-131 for treatment of graves disease discovers that she is pregnant. Which of the following is a known complication
   A. Fetal cretinism B. Fetal retinoblastoma
   C. Childhood leukemia D. None
9. Which of the following is assosiated with FGR
   A. Metoclopromide B. Low dose asprin
   C. Clexane D. Cyclophosphomide
10. Antenatal use of nitroglycerine to control severe maternal hypertension can lead to which of the folowing complication
    A. Fetal acidosis B. Fetal cyanide toxicity
    C. Fetal oliguria D. Reduced heart variability on NST

Watch out for the answers in the next issue

Association of Obstetricians & Gynaecologists of Delhi

MEMBERSHIP FORM

Name:.....

Surname: .....

Qualification (year): .....

Postal Address: .....

City:..... State: ..... Pin code: .....

PHOTO

Place of Working: .....

Residence Ph. No. ..... Clinical / Hospital Ph. No. .....

Mobile No:..... Email: .....

Gender: Male:..... Female:.....

Date of Birth: Date.....Month ..... Year.....

Member of Any Society:.....

Proposed by .....

Cheque/DD / No: .....

Cheque/Demand Draft should be drawn in favour of:
AOGD 2024

FOR ONLINE TRANSFER THROUGH NEFT/RTGS

Name of Bank: Bank of Baroda
Branch: Dr RML HOSPITAL DELHI
Name of Account: AOGD 2024
Account no: 26020200000452
IFSC code: BARB0RAMDEL
MICR code: 110012061

For Life Membership : Rs. 11,000 + Rs. 1,980 (18% GST applicable) = Rs. 12,980For

New Annual Membership* : Rs. 2,000 + Rs. 360 (18% GST applicable) = Rs. 2,360

For Old Renewal Membership+ : Rs. 1,200 + Rs. 216 (18% GST applicable) = Rs. 1,416

Encl.: Attach Two Photocopies of All Degrees, DMC Certificate and Two Photographs (Self attested)

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+ - In case of renewal, mention old membership number.Note: 18% GST will be applicable as FOGSI requires it.

Send Complete Membership Form Along With Cheque / DD and Photocopy of required documents.

AOGDtiOffice, Department of Obstetrics & Gynaecology, Maternity Nursing Home,ABVIMS & Dr RML Hospital, New Delhi- 110001

Contact: 01123404419. Mob :+91 97173 92924

AOGD 2024

46th Annual Conference of AOGD

Organised By:

Atal Bihari Vajpayee Institute of Medical Sciences & Dr. Ram Manohar Lohia Hospital, New Delhi

Theme:

Shared Decision Making - Enhancing Women Emancipation

22nd 23rd 24th NOVEMBER, 2024

Early Bird Registration till 31st July, 2024

Register Now!

AOGD Member	INR 7080
Non Member	INR 8260
PG Students	INR 5900
Accompanying Person	INR 5900
1 Workshop Fee	INR 2360
2 Workshop Fee	INR 2950

Inclusive of 18% GST

Scan QR Code to Register

Venue: India Habitat Centre, Delhi

AOGD 2024

46th Annual Conference of AOGD

Organised By:
Atal Bihari Vajpayee Institute of Medical Sciences &
Dr. Ram Manohar Lohia Hospital, New Delhi

22nd, 23rd & 24th November, 2024 | Venue: India Habitat Centre, Delhi

Theme: Shared Decision Making - Enhancing Women Emancipation

Registration Form

AOGD Member: Yes ◯ No ◯ AOGD Membership No. _____ DMC No. _____

Title: Prof. ◯ Dr. ◯ Mr. ◯ Ms. ◯ Mrs. ◯ **Gender:** Male ◯ Female ◯

First Name **Middle Name** **Last Name**

Address:

Country: **City:** **State:** **Pin:**

Telephone: **Mobile No. with Country Code:**

Email:

(Fill the Form in Block Letters Only) *(All the above fields are mandatory)*

Pre-Conference Workshops - 22nd November

Registration Fees

Category	Early Bird (Till 31st July, 2024)			Regular (1st Aug to 31st Oct, 2024)			From 1st November, 2024 Onwards/On-spot		
	Amount	GST 18%	Total	Amount	GST 18%	Total	Amount	GST 18%	Total
☐ AOGD Member	6000	1080	**7080**	6500	1170	**7670**	7000	1260	**8260**
☐ Non Member	7000	1260	**8260**	7500	1350	**8850**	8000	1440	**9440**
☐ PG Students	5000	900	**5900**	5500	990	**6490**	6000	1080	**7080**
☐ Accompanying Person	5000	900	**5900**	5500	990	**6490**	6000	1080	**7080**
☐ 1 Workshop Fee	2000	360	**2360**	2250	405	**2655**	2500	450	**2950**
☐ 2 Workshop Fee	2500	450	**2950**	2800	504	**3304**	3000	540	**3540**
☐ AOGD Member (Above 75 year)	**Complimentary** (Kindly email duly filled Registration Form along with age proof on our official email id mentioned below)								

Registration Includes

- Lunch on Conference Days
- Tea / Coffee Served During the Conference
- Conference Sessions
- Inaugural & Valedictory Functions
- Entry for Trade/Exhibition Area
- Conference Kit

Note:
- Post graduates to attach a certificate from HOD and also should be a member of the AOGD in order to attend and present a paper.
- Membership number is mandatory for registration in membership category
- For spot registration: payment will be accepted only by mode of Cash/Card/UPI. The disbursal of Delegate kit for the same will be subject to availability
- Delegate kit would be handed over only to registered delegate
- Registration is non transferable
- Post conference, no kit or any workshop material will be disbursed to the Delegate/associate Delegate/PG student

For Offline Payment

1. All DD/Cheque payable at New Delhi & should be made in favour of "**AOGD 2024**".

Write your Name and Contact No. at the back of DD/Cheque.

Cheque should be deposit in **AOGD Secretariat, Department of Obstetrics & Gynaecology Maternity Nursing Home**
Atal Bihari Vajpayee Institute of Medical Sciences & Dr. Ram Manohar Lohia Hospital, New Delhi - 110001
Email: aogdrml2024@gmail.com | Mobile: +91 9717392924 | Phone: 01123404419

Offline Payment Details

DD/Cheque No. .....Dated: .....

Drawn on (Name of the Bank).....Branch.....Amount.....

Bank Transfer Details

Account Name: AOGD 2024

Account No.: 26020200000452

Bank: Bank of Baroda

Branch: Dr RML Hospital Delhi

IFSC Code: BARB0RAMDEL

MICR Code: 110012061

Mode of Payment.

- ☐ Cash
- ☐ Card (Debit/ Credit)
- ☐ Demand Draft
- ☐ Cheque
- ☐ Online
- ☐ NEFT

UTR/Reference Number/Transaction Id: .....

For Online Registration Click Here

Scan QR Code to Register

Cancellation & Refund Policy

1. All cancellation should be made in writing and sent to AOGD secretariat.
2. All cancellation received on or before 31st July 2024 will be entitled for 75% refund of the amount paid.
3. All cancellation received between 1st August 2024 to 31st October 2024 will be entitled for only 25% refund of the amount paid.
4. No refund for cancellation made on or after 1st November 2024.
5. The refund process will begin only 30 days after the completion of the conference.

AOGD Office

Secretariat Address
Department of Obstetrics & Gynaecology
Maternity Nursing Home
Atal Bihari Vajpayee Institute of Medical Sciences &
Dr. Ram Manohar Lohia Hospital, New Delhi - 110001
Email: aogdrml2024@gmail.com
Mobile: +91 9717392924 | Phone: 01123404419

Congress Manager

Conferences International
B-220/2, Second Floor,
Opposite Kali Masjid
Savitri Nagar - 110017
New Delhi | India
M: +91 9560493999
Email:----------

- AOGD 2024: organizing committee shall not be liable for failure or delay to organize the AOGD 2024 conference, which may become practicably impossible because of circumstances beyond the reasonable control of the organizing committee. Such circumstances include without limitation natural disasters or acts of god, acts of terrorism, labor disputes or stoppages, war.

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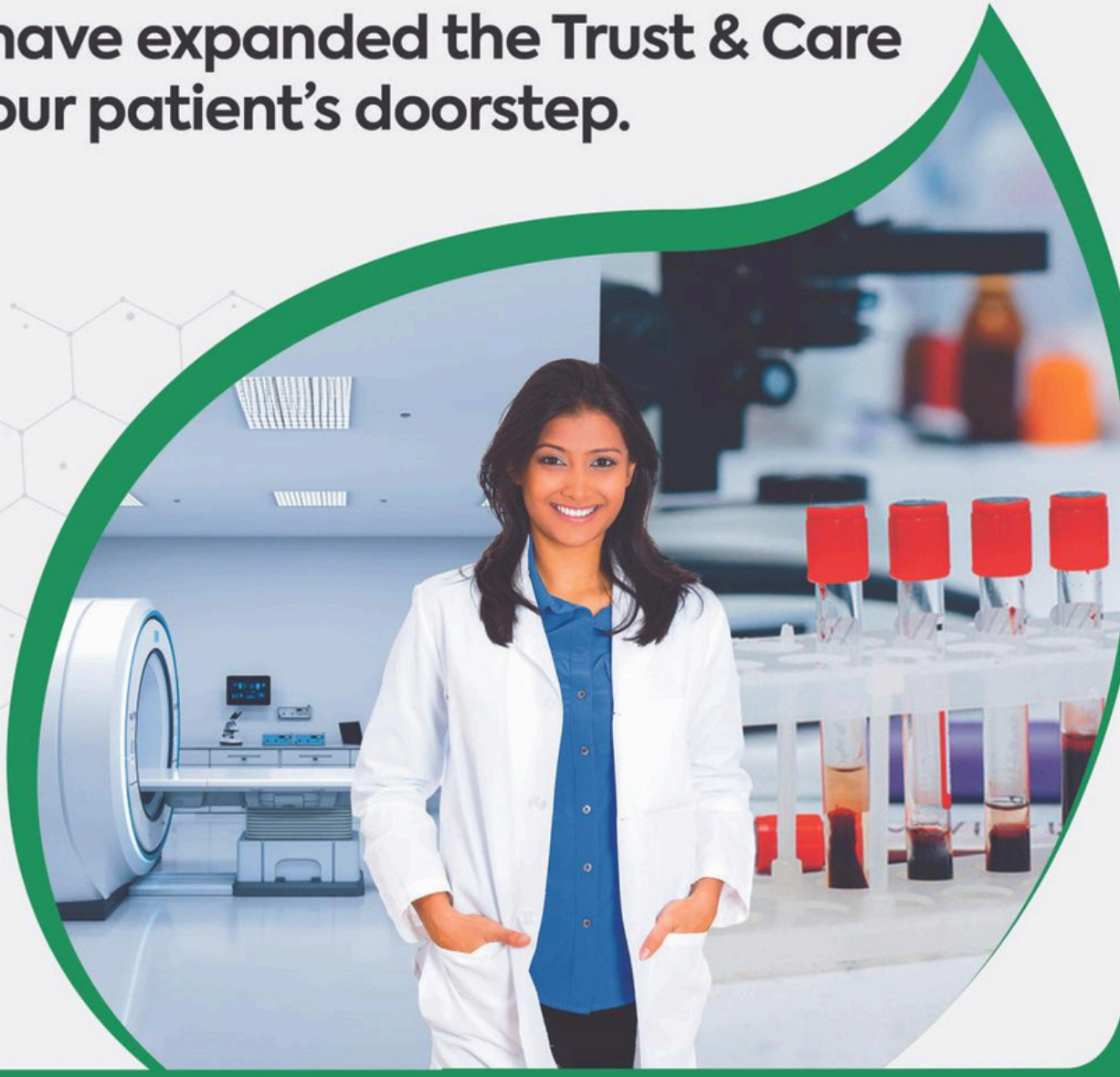

LOCATIONS

- Safdarjung Development Area
- Defence Colony
- Gurugram
- Pusa Road
- Bali Nagar

Scan for appointments & queries

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