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ICOG
CAMPUS

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PERINATALOGY

ICOG - Chairperson
Dr. Mandakini Megh

FOGSI - President
Dr. Alpesh Gandhi

ICOG - Secretary
Dr. Parag Biniwale

Editorial Team
Chief Editor : **Dr. Mandakini Megh** | Issue Editor : **Dr. Chinmayee Ratha**

Indian College of Obstetricians and Gynaecologists of The Federation of Obstetric and Gynaecological Societies of India

ICOG was created to promote education, training, research and spread of knowledge in the field of Obstetrics and Gynaecology, Family Welfare and other related areas for students and specialists involved with or interested in women's health care and to address the academic requirements of FOGSI members.

ICOG Invites the Applications for-

1. Online Fellowship of ICOG (FICOG): Should have MD/DGO or equivalent qualification for 10 years, Membership of FOGSI for 5 years, Publication of 3 papers in any reputed Journal / Newsletter / FOGSI Focus etc in the last 10 years or 100 ICOG Credit Points over any 3 years, Attendance of 2 FOGSI sponsored Congresses in the last 10 years, Presentation of atleast 2 papers at FOGSI / FIGO / AOFOG / National / State Level Congresses as 1st author in the last 10 years, Fellowship payment of Rs.15,500/- online." Last date is October 31. Only Fellow can get chance as a invited speaker for ICOG CME's, Dr. Usha Saraiya Oration organized by member societies of FOGSI as well as for ICOG Dr. C. L. Jhaveri Symposium during AICOG. Also only ICOG Fellow can contest the Election of ICOG. **2. CME:** For 1 or 2 days with FOGSI Society and funds from ICOG will Rs. 25,000/- for one day or Rs. 50,000/- for two days partly. **3. Credit Points:** FOGSI affiliated societies will get ICOG Credit Points free with programme. Other than FOGSI affiliated societies like ISAR, ISOPARB, ISAP, IMA and other registered organizations will be charged by a Demand Draft in favour of FOGSI as Half day programme- Rs. 7,500/-;Full day programme- Rs. 15,000/-;Two days programme- Rs. 25,000/-;Three days programme- Rs. 30,000/-. **4. Emcure Pharma Travel Award:** Member or Fellow of ICOG can apply for ICOG Emcure Travel Award so that he/she can take short term training of about 2-4 weeks anywhere in India. Last date is March 31. **5. Two Visiting Professorship** from ICOG to any Teaching Institute (Medical College) for five days in India in coordination with FOGSI society. Funds from ICOG Rs. 15,000/- for each Professor. **6. Online course in Contraception and Family Welfare 7. ICOG Violence against Women Training Course. 8. ICOG certificate course in Adolescent Health.**

Regarding MRCOG Part 1 Revision course- ICOG takes pleasure to inform you that combined MICOG-MRCOG Part 1 examination is being held in India since 2013 twice in a year to help our students for preparation. All those interested, please visit RCOG website www.rcog.com to do all formalities regarding examination and then apply for MICOG for that you need to send a DD of Rs. 20,000/- in favour "FOGSI" as MICOG fee with photocopy of application form, MBBS certificate and FOGSI membership. This fee will include preparatory session of three days conducted by experienced teachers from India and abroad. 16th Refresher Course will be held in May 2020 at FOGSI Office, Mumbai between 9.00 am to 6.00 pm. Exact date will be announce in due course.
Regarding MRCOG Part 2 Revision course- Dates will be announced on the ICOG website as well as send the SMS to all FOGSI members.

ICOG Recognized Training Centres for Six months-

A.Reproductive Medicine
1.Dr. Asha Rao, Coimbatore
2.Dr. Anjalakshi Chandrasekar, Chennai
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17.Dr. Urmila Somen, Cochin
18.Dr. Vidya V Bhat, Bengaluru
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C.Ultrasound
1.Dr. Meeta, Hyderabad
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D.Fetal Medicine
1.Dr. Chinmayee Ratha, Hyderabad
2.Dr. Jayprakash Shah, Ahmedabad
3.Dr. Prashant Acharya, Ahmedabad
4.Dr. Selvapriya Saravanan, Nagercoil

E.Vaginal Surgery
1.Dr. Kawita Bapat, Indore

F.Critical Care in Obstetric
1. Dr. Girija Wagh, Pune
2. Dr. Pratima Mittal, New Delhi

Important Notes: 1. FICOG will be granted only in person in ICOG Convocation during AICOG. 2. AICOG conference registration is compulsory to attend the ICOG Convocation. 3. For MICOG, candidate appear for the MRCOG & MRCPI exams and after clearing the exams, they can get MICOG in ICOG Convocation during AICOG. 4. Those who cleared the MRCOG Part 1,2,3 and would like to have MICOG,on payment of ICOG fee and an interview by ICOG office bearers, they can be awarded MICOG in ICOG Convocation during AICOG.

For more details, please send email to icogoffice@gmail.com / icog@fogsi.org or visit the ICOG website www.icogonline.org

Enhanced workload sharing and greater participation of GC members

Streamlining the ICOG Office activities by an adequate delegation of duties is long overdue as the workload of ICOG has considerably increased. Involvement of G C Members in the CMEs, Conferences Examinations & YUVA FOGSI will be further enhanced this year. We are planning to update the directory of members and fellows. International Courses - MRCOG & European Board of College course will help with global collaborations and better standards. The aim is to popularize ICOG Training Courses & wide publicity to the Training Courses for deserving candidates. Overall, to make the activities of ICOG more-user-friendly and ICOG Office more approachable. Review meetings of ICOG office bearers, YUVA FOGSI, and meetings will be at FOGSI Conferences. Training Centre heads meeting will be held in April & September.

Progressive, futuristic, technology-driven plans

In this era of digital visibility, we shall also be working on the website making it more vibrant so that ICOG fellows & members can access relevant information at a click. We are in the process of having ICOG credit points, FICOG applications online. Online certification course on Contraception and family welfare was launched at Lucknow recently and soon, we shall be rolling out an online course on Domestic & Sexual Violence against Women. Clinical Research in another area where ICOG plans to venture into.

PUBLICATIONS:

Year Book 2020.
Release of Book – Updates –Text Book of Playing by Rules: An update on Government Policies Regulations and acts for Practicing Obstetricians and Gynecologists
ICOG-CAMPUS – our regular journal will be released on schedule. This issue on perinatology is for your perusal and I hope you find it useful. I will continue to communicate with you through this journal section called “Chairperson ke mann ki baat” !!

SAVE THE DATES:

The FOGSI ICOG National Conference 2020 will be held on 4th 5th & 6th December 2020 at Taj Santacruz, Mumbai. The theme of the Conference will be “Prevention, Prediction & Practices In Non-Communicable Diseases.” With adequate notice, I am sure all of you can plan to be part of this very important academic get together.

There is lots to do and very little time to do it all. Yet each step matters in a long journey.
“Coming together is a beginning, working together is progress….”

I look forward to this journey together.

Yours Sincerely,

Mandakini Megh

President’s Message

Dr.Alpesh Gandhi
President, FOGSI

At the outset, I wish all FOGSIANS a happy new year 2020. With the motto of “safety first”, I envisage a year of academic and administrative endeavours furthering this cause. I am happy to see an issue on Perinatology in the ICOG campus because this is an area where the parameters of safety are of utmost importance not only to the mother and fetus directly, but also to the family and society as a whole. Any serious catastrophe in the perinatal period can have widespread implications.

The need to standardise management protocols in this area is immense and it usually requires a “team approach” as many stakeholders are involved. This edition of the newsletter is dedicated to the very enigmatic topic of “Perinatology”, including an article on “simulation training in neonatal resuscitation” that is a practical innovative solution to a situation that stumps even the most experienced Obstetricians. We begin the New Year with this evolving topic to steer your thoughts in a positive direction and empower you to tackle the challenges of the ever expanding horizons of Obstetrics.

Happy Reading!

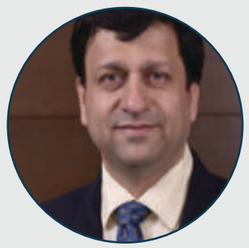
ICOG Office bearers 2020

ICOG Team 2020

Dr. Alpesh Gandhi
President FOGSI

Dr. Mandakini Megh
Chairperson ICOG

Dr. Parul Kotdawala
Vice Chairperson ICOG



Dr. Parag Biniwale
Secretary ICOG

Dr. Uday Thanawala
Chairperson Elect

Governing Council Members: 2018 to 2020

Dr. Ameet Patki, Mumbai	Dr. M. Krishna Kumari	Dr. Sadhana Gupta
Dr. Anita Singh, Patna	Dr. Madhuri Chandra	Dr. Sarita Bhalerao
Dr. Archana Baser, Indore	Dr. Mandakini Megh	Dr. Sheela Mane
Dr. Asha Baxi, Indore	Dr. Murlidhar Pai	Dr. T. Ramani Devi
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Dr. Girija Wagh	Dr. S. Sampathkumari	

MANN KI BAAT

Chairperson Ke Mann Ki Baat...

Dr. Mandakini Megh
Chairperson, ICOG 2020

My Dear ICOGians,

At the outset, I thank you very much for electing me as the CHAIRPERSON of ICOG 2020. It is a matter of great privilege to take this responsibility in an institution that I have served diligently in escalating capacities since the early days of my career as an ObGyn specialist. I am overwhelmed to have been bestowed this honour this year and I promise you to strive to do my best to do justice to this post.

The college was established with the aim of promoting education, training and research in the field of Obstetrics, Gynaecology, Reproductive health, Family Welfare and emerging related sub-specialties. In furtherance of these objectives, this year our team will be actively involved in the National Family Welfare programs and I sincerely advise all Fellows to actively associate and co-operate with Central and State Government Health authorities and corporate bodies in implementing all national programs of Family Planning including training of Paramedical and Health personnel.

The annual theme of ICOG this year spells “Equip. Educate. Empower”. In 2020, under the leadership of President Dr. Alpesh Gandhi and myself, we shall be particularly aiming to:

- Equip our ObGyn fraternity with the skills to deal with challenges of day-to-day practice.
- Educate our colleagues with updates in the subject-related knowledge base.
- Empower the members with state of the art knowledge & skills and training.

The aim of this year is the standardization of clinical practice by bringing together teachers from Medical colleges all across the country. These Professors will brainstorm and help us create Good Clinical Practice Recommendations as envisaged by President Dr. Alpesh Gandhi. Thus, we hope to have a positive impact on patient care & evidence-based management. As a prelude to these targets, I have set up on a journey with some small steps to start with :

Tribute to our past leaders

The heights we achieved today have been facilitated by the academic giants who “shouldered” the responsibility of guiding us towards excellence. As a mark of respect to our founding fellows, we felicitated ICOG legends for their Life Time Services as Dr. Rohit Bhatt, Dr. Shirish Daftary, Dr. Shirish Sheth, Dr. Usha Krishna, Dr. Usha Saraiya, Dr. C. B. Purandare, Dr. Meera Agnihotri, Dr. Rangila Sinha and Dr. Raj Baveja along with our recent Past Chairpersons at ICOG Convocation on 01.02.2020 during 63rd AICOG at Lucknow, Uttar Pradesh.

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Past Chairpersons

Late Dr. C. L. Jhaveri Mumbai (1989-96)	**Dr. Duru Shah** Mumbai (2009-2010)	**Prof. Krishnendu Gupta** Kolkata (2016)
Late Dr. C. S. Dawn Kolkata (1997-1999)	**Late Dr. Behram Anklesaria** Ahmedabad (2011)	**Dr. Mala Arora** Faridabad (2017)
Late Dr. Behram Anklesaria Ahmedabad (2011)	**Dr. A. K. Debdas** Jamshedpur (2012)	**Dr. S. Shantha Kumari** Hyderabad (2018)
Dr. Mahendra N. Parikh Mumbai (2000-2002)	**Dr. Hiralal Konar** Kolkata (2013)	**Prof. Tushar Kar** Odisha (2019)
Dr. Rohit V. Bhatt Baroda (2003-2005)	**Dr. Atul Munshi** Ahmedabad (2014)	
Dr. Usha B. Saraiya Mumbai (2006-2008)	**Dr. Dilip Kumar Dutta** West Bengal (2015)	

Past Secretaries

Dr. Sanjay Gupte Pune (2006 -2008)	**Dr. Jaideep Malhotra** Agra (2012-2014)
Dr. Hema Divakar Bangalore (2009-2011)	**Dr. S. Shantha Kumari** Hyderabad (2015-2017)

Chairperson's Message

Dr. Mandakini Megh
Chairperson , ICOG

Happy New Year 2020 !!
It brings me great pleasure to present to you all the issue of ICOG Campus on "Perinatology". My motto as chairperson of this esteemed college this year is to "Educate, Equip and Empower" the ICOGians with knowledge and skills that will help them combat the challenges posed by complex clinical scenarios in their day to day lives.
In this endeavour, I conceived the idea of having an issue on a topic that includes the combined problems of high risk Obstetrics, delivery period challenges as well as neonatal care issues. Perinatology envisages the entire realm of safe motherhood and healthy neonates. We have carefully handpicked the topics to cover the range of clinical possibilities and although it is not possible to cover each and every topic in a small newsletter, an attempt has definitely been made to provide an insight into the possible broad areas in perinatal care

We have roped in multidisciplinary inputs and highlighted the fact that without such a "teamwork" meaningful perinatal care is not possible. I thank Dr. Chinmayee Rahtha for her efforts in putting together this issue of ICOG campus. I hope the readers find this exercise useful. I look forward to a very eventful year and solicit your participation in all our academic activities.
Happy Reading!

aortic stenosis with left ventricular dysfunction. Preliminary data suggest that this intervention may prevent progression of aortic stenosis into a more ominous form of heart disease, hypoplastic left heart syndrome [18]. Fetal balloon pulmonary valvuloplasty also has been successfully performed for fetuses with critical pulmonary stenosis [19]. At present, the scope of fetal cardiac interventions in developing countries is very limited.

Conclusions

The availability of fetal echocardiography has provided a very unique opportunity to diagnose and understand various forms of congenital heart disease from early gestation. Prenatal diagnosis of CHD and planned delivery in a cardiac facility results in excellent immediate outcomes in neonates receiving specialized post-natal cardiac care . There is a pressing need to diagnose complex CHD in early pregnancy through better ultrasound screening, providing more options to expectant families. A multi-disciplinary team approach is required to for diagnosis, counseling and perinatal care in order to provide the most appropriate management strategy and optimize pregnancy and neonatal outcomes [20].

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resulting in duct dependent systemic circulation – this includes conditions like Critical aortic stenosis, severe coarctation of aorta, interrupted aortic arch etc.

An excellent co-ordination between all concerned specialties (Cardiology, obstetrics, cardiac surgery, neonatology, anesthesia, nursing and counselor) is required to ensure that there is a smooth transition of care for these critically ill infants.

Timing of Delivery: The delivery date is planned in co-ordination with the pediatric cardiologist and cardiac surgeon to ensure that corrective intervention is carried out in a timely fashion. In most fetuses with CHD, delivery near term is ideal unless there is a very clear fetal or maternal indication. The outcomes of neonatal heart surgery are significantly influenced by premature delivery.

Mode of Delivery: The mode of delivery can be tailored according to the obstetric requirements and most of these infants tolerate normal vaginal delivery. The American Heart Association has published indications for consideration of planned caesarian section in fetuses with CHD [6]. These include transposition of great arteries with restrictive PFO or ductus arteriosus, Hypoplastic left heart syndrome with restrictive PFO, Obstructed total anomalous pulmonary venous drainage, Severe valve regurgitation with hydrops and uncontrolled fetal arrhythmias.

Site of Delivery: Planned delivery in a pediatric cardiac facility avoids neonatal transport of an infant with critical CHD and ensures prompt initiation of cardiac care in order to maintain the in-utero shunts like prostaglandin infusion or balloon atrial septostomy. We have reported the feasibility of this strategy in limited resource settings with beneficial impact on the immediate outcomes after neonatal surgery [14]. Recently, we reported that the strategy of prenatal diagnosis and planned delivery significantly improves pre-operative clinical status in neonates with critical CHD and reduces the length of hospital stay before definitive surgical repair [15]. This resulted in improved surgical outcomes and can possibly have a significant impact on the costs of in-hospital care by lowering the duration of ICU and hospital stay. It is possible that this strategy can have a beneficial impact on long-term neurodevelopmental outcomes after cardiac surgery by reducing the degree of hypoxia and metabolic insult in the pre-operative period.

Option III – In-Utero Therapy

There are limited situations where in-utero therapy can be offered when a diagnosis of heart disease is made by fetal echocardiography. This includes:

1. Rhythm disorders
2. Selected structural heart disease – fetal interventions.

Rhythm Disorders

This includes fetuses diagnosed with various types of tachy and Brady arrhythmias.

a. **Tachycardias** - The most common forms of tachyarrhythmias in the fetus include supraventricular tachycardia and atrial flutter. Most of these arrhythmias are diagnosed between 20 – 30 weeks of gestation. There is a risk of development of fetal hydrops, especially if the tachycardia persists for longer periods of time. Many of these tachycardias can be effectively managed using trans-placental therapy [16]. The various drugs given to the mother include digoxin, flecanaide, sotoalol, amiodarone etc. In most situations, therapy is initiated after hospitalization of the mother, with frequent monitoring of the fetal rhythm and maternal ECG. Frequent monitoring of both the mother and the fetus is required. In most cases, it is possible to effectively control the tachycardia and continue pregnancy till term. Most infants require continued medications after birth for a period of 6-12 months.

b. **Bradycardias** - The most significant bradyarrythmia that requires treatment in utero is congenital complete heart block. Many cases are associated with maternal auto-immune disease (SS-A/SS-B antibodies). Since transplacental transfer of these antibodies occur principally after 18 weeks, most of these cases manifest by around 20-24 weeks. Heart rates of < 55 beats /minute are often associated with hydrops and very high incidence of fetal demise. Trans-placental therapy is possible with maternal steroids (dexamethasone) in conjunction with beta-agonists. Recent studies have reported very good outcomes with such therapy and a very good number of fetuses can be managed till term when they are electively delivered and a pacemaker is implanted in the neonate [17].

Fetal Interventions for structural heart defects:

At present, the scope of fetal interventions is limited to very few conditions especially severe obstruction to the outflow tracts. The most common fetal intervention reported is fetal balloon aortic valvuloplasty for critical

Secretary's Message

Happy New Year 2020 to all the readers

It gives me great pleasure to see that we are addressing the topic of "Perinatology" in this issue of the ICOG campus. Perinatology includes the clinical aspects of Obstetrics, Fetal Medicine and Neonatology as a continuum of care. The concept has now evolved so rationally that all clinicians have come to appreciate Perinatology as a science in itself.

The ICOG campus has become a popular ready reckoner for challenging clinical topics for all FOGSIans and the readership is constantly on the lookout for meaningful articles that help update our understanding of complex situations in this ever-evolving field of ObGyn.

The topics on various aspects of perinatal care along with inputs from pediatric cardiologists and neonatologists are very inspiring. Multidisciplinary care is the need of the hour and I am sure this issue will make for an interesting read through some unique scenarios which have been presented by the experts in their field in a rather simple and practical format. I would like to compliment Dr Chinmayee Ratha who has chosen topics and authors carefully to compile this issue of ICOG campus. It will really serve the purpose of "Equip , Educate and Empower" for the readers and they would be immensely benefited by this publication.

Happy reading!

Dr.Parag Biniwale
MD, FICOG
Secretary, ICOG

From the Editor's Desk

Dr. Chinmayee Ratha
MBBS, MS - Obstetrics & Gynaecology, MRCOG, FIMSA, FICOG
Fetal Medicine Consultant - Navodaya Hospital

At the outset, I thank the chairperson of ICOG - Dr Mandakini Megh madam, for this splendid opportunity of putting together an issue of the ICOG Campus on Perinatology. The science of "perinatology" is one of the most exciting branches of our clinical practice as ObGyn. It not only crosses the barrier of individual disciplines and extracts expertise from a conglomeration of subspecialities but also literally addresses multiple patients in one go. We always have one mother and at least one fetus (making it at least two patients at a time !!) and sometimes many foetuses together.

Many experts get together and form a team to provide the best that medicine can offer to a mother at the brink of delivery and help optimise the most difficult journey of a tiny human being. Good perinatal care is the cornerstone of ensuring healthy mothers and safe childbirths not only in preventing obstetric trauma but more importantly ensuring "intact survival" and a power to overcome congenital problems.

I thank all the authors who have made a tremendous effort, despite each one's own gruelling time schedule, to collate recent evidence and their own experience in preparing these formidable write ups about challenging topics. It is laudable that the ICOG provides us this common platform to present our ideas facilitating an excellent peer group interaction. I particularly thank Dr Parag Biniwale, the dynamic secretary of ICOG, for his constant support and solutions to our multiple queries which has helped bring this issue out in time.

We are standing at the edge of a frontier today – filled with numerous possibilities ahead and the only effective way to move forward from here is to equip, educate and empower ourselves with information that is up-to-date, practical and rational. Perinatology is coming of age with every clinician in ObGyn realizing that we cannot practice in solitary confinement of our science – multidisciplinary team approach is the need of the hour and no other science defines, justifies and exemplifies this better than Perinatology! Neonatologists are breaking barriers in the limits of viability, pediatric subspecialists are keen on getting involved antenatally so that the continuity of care delivery is established early and "golden opportunities" are not lost in terms of time frames.

You will find articles in this issue addressing some vital topics in perinatal care that will help you move a step forward in your own clinical practice. Ideas like "simulation training" for neonatologists should inspire Obstetricians to motivate their individual neonatologists to acquire necessary skills through such modules. This will go a long way in empowering even smaller service delivery units.

"We live in interesting times…" said Albert Einstein – though I will never know exactly what he was referring to but the genius that he was, I know that this statement stands true almost for every happening moment. Yes, a lot has been done and a lot is still waiting to happen. In Perinatology, we may not be able to "cure" everything but we certainly can "care" for all. We begin this new year, this new decade with a resolution – we will stay aware and awake to the changes around us. I hope you find this issue interesting to read.

Keep thinking , keep reading - to think again!!

Options for Management After Prenatal Diagnosis of CHD

This can be discussed under the following headings:

1. Situations where the option of medical termination of pregnancy may be discussed with the family.
2. Planned delivery and peri-partum care.
3. Role of in-utero treatment (trans-placental therapy or fetal cardiac intervention)

Option I – Medical Termination of Pregnancy

Though a very disappointing option for expectant parents, medical termination of pregnancy maybe a practical option for most Indian families in certain forms of CHDs. These conditions typically are not amenable for a complete correction and only palliative surgical treatment can be offered. Counseling for termination of pregnancy has to be in accordance with the local, regional, and national rules and regulations. In India, the diagnosis of CHD needs to be confirmed before 20 weeks (the legal limit for termination of pregnancy) for this option to be practicable [11]. The role of the fetal specialist and obstetrician is to prognosticate the outcomes in these situations and let the family take the final decision regarding pregnancy management, including the option of termination of pregnancy.

Examples of Such Conditions Include:

- Hypoplastic left heart syndrome.
- Complex forms of single ventricle physiology (associated with abnormalities of pulmonary veins, pulmonary atresia and abdominal situs). These conditions are often classified under the category of "Heterotaxy" or "isomerism" anomalies.
- Complex form of pulmonary atresia with non-confluent pulmonary arteries and aorto-pulmonary collaterals.
- Severe regurgitation of atriventricular valves with hydrops – classical examples include Ebstein's anomaly of tricuspid valve, Pulmonary atresia-intact ventricular septum with severe TR and right ventricular dysfunction.
- Complex heart disease associated with major rhythm abnormalities like complete heart block Eg: Left Isomerism.
- Congenital heart defects associated with major extra-cardiac or genetic abnormalities.

Many of these lesions require multiple staged palliative procedures after birth, very often starting from the neonatal period. Frequent follow-up visits and diagnostic procedures are required in the interim periods. Medications like anticoagulation therapy with monitoring is required for these patients for a long period of time. In addition, there is a significant risk of long-term complications on follow-up necessitating hospitalizations and further interventions. Many of these patients face significant challenges in growth and neurodevelopment which make care of these patients very challenging. In view of these multiple reasons, it is very important for obstetricians to ensure that these types of complex CHDs are detected very early in pregnancy by ensuring timely referral for fetal heart evaluation so that all options for pregnancy management maybe presented to the expectant families.

Option II – Role of Planned Delivery and Peri-Natal Care:

This scenario applies to those cardiac conditions that are potentially lethal in the neonatal period without intervention and where corrective surgery offers excellent long-term outcomes. In most of these conditions, the survival of the infant depends on the continued patency of the arterial duct after birth to maintain pulmonary or systemic blood flow. This is accomplished by starting an infusion of prostaglandin E1 after birth when indicated. Once the duct starts to close, these babies can present with severe cyanosis or shock. It maybe extremely hazardous to transport such sick babies to a tertiary care pediatric cardiac facility after they have started showing symptoms. Hence, in such conditions the best possible option after pre-natal diagnosis would be to plan delivery in a center with pediatric cardiac facility so that immediate care can be delivered to the baby after birth. Studies have shown that such a strategy may improve outcomes in babies with critical forms of CHD [12-13].

Examples of cardiac conditions where in-utero transport and planned delivery maybe considered:

- Transposition of great arteries (especially with intact ventricular septum) – baby may require an emergency post-natal intervention called balloon atrial septostomy to correct hypoxemia followed by the corrective arterial switch operation.
- Critical obstruction to right ventricular outflow tract resulting in duct dependent pulmonary circulation – this includes conditions like critical pulmonary stenosis/pulmonary atresia, Tetralogy of Fallot and allied physiologies.
- Critical obstruction to left ventricular outflow tract

Table III: Congenital Hearts Defects in Fetus Based on Prognostication

CHD	View for Detection	Genetic Associations	Prognosis
Septal defects Coarctation TAPVC	4 chamber view 3 vessel view.	AV septal defect – Trisomy 21	Excellent Single staged repair.
TOF, TGA, DORV (most forms)	Outflow and 3-vessel view	TOF, DORV – 22q deletion syndrome, Trisomies	Good with > 95% long-term survival. Single staged repair. Low risk of re-operations.
TOF-PA, CAT, TA, DILV, DORV (complex), PA-IVS.	All views	22 q deletion in TOF-PA, CAT.	Fair prognosis > 90% adult survival. Needs multiple staged operations.
HLHS, Isomeric hearts, Complex pulmonary atresia, Severe Ebsteins	All views	22 q deletion in pulmonary atresia.	Guarded prognosis. Multiple staged operations. Long-term medications.

Four-Chamber View: This enables detection of most forms of complex heart defects of the anatomic or functional single ventricle physiology. In simple terms, the 4-chamber view permits categorization of heart defects into those which can be offered anatomic correction (CHDs associated with 2 adequately sized ventricles) versus those in which only staged palliative procedures can be offered (CHDs associated with hypoplasia of the ventricles). This includes conditions like hypoplastic left heart, isomeric hearts with unbalanced ventricles and hearts with univentricular circulation.

Outflow Tracts and 3-Vessel View: These views enable diagnosis of abnormalities of outflow tracts and great vessels including critical obstructions of the outflow tracts. Major obstructive lesions are associated with reduction in size of the corresponding outflow in 3-vessel view and abnormal color Doppler flow patterns (like reverse flow) in the arches in 3-vessel tracheal view. Many of these conditions have a normal 4-chamber view and hence total correction is feasible with favorable long-term prognosis. Examples of CHDs detected by outflow tract and 3 vessel views include Tetralogy of Fallot, Transposition of great arteries and Coarctation of Aorta.

Evaluation of the Fetal Heart Rate and Rhythm: This can be done using Spectral Doppler and M-mode in special situations. Besides the fetal heart rate, a basic evaluation of the atrio-ventricular relationship (rhythm) is necessary. The normal fetal heart ranges from 120-180 beats per minute with a 1:1 atrio-ventricular relationship.

Counseling after Diagnosis of Congenital Heart Disease by Fetal Echocardiography.

The principal role of a pediatric/fetal cardiologist comes after the diagnosis of a congenital heart disease has been made in utero. The counseling plan has to be individualized and a different strategy maybe followed for various families depending upon their financial and social background. Most forms of congenital heart disease can be effectively corrected or palliated in early life with very good outcomes. Several centers in India are now undertaking complex surgical procedures in very tender hearts with excellent short-term and intermediate outcomes [10]. However, it is generally agreed that the prognosis even after palliation is suboptimal for very complex forms of congenital heart disease (typically the single ventricle heart) and if the cardiac lesion is associated with major extra-cardiac or genetic abnormalities.

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Liver Disorders In Pregnancy

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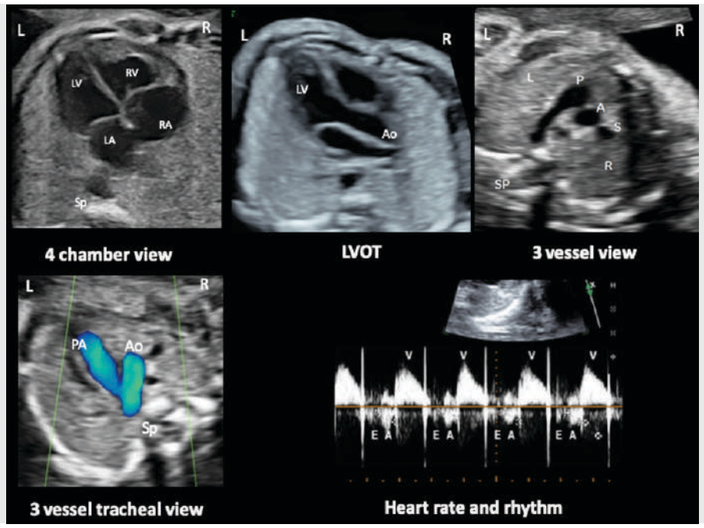
Figure 1: Common Views for Fetal Heart Screening.



LA- Left atrium, RA- Right atrium, LV- Left ventricle, RV- Right ventricle, Sp- Spine, A, Ao- Aorta, P, PA- Pulmonary artery, S- Superior vena cava, L- Left, R- Right. Doppler – E and A represent early and late diastolic filling atrial waves and V the systolic ventricular waveform.

A Simplified Approach to Fetal Diagnosis of CHD:

Various systems of classification are available for congenital heart disease. Using a basic protocol for fetal heart screening (a combination of 4 chamber, outflow tract and 3-vessel views), it is possible to diagnose most forms of major CHD (Table II). Table III summarizes common types of CHDs based on their complexity and is useful for the purpose of prenatal counseling.

Table II: Cardiac Conditions which can be Diagnosed by Fetal Echocardiography

4 Chamber View	Outflow Tract and 3-Vessel Views
1. Major septation defects 2. Significant chamber hypoplasia (HLHS/PA-IVS) 3. Major valve atresia/stenosis. 4. Ventricular dysfunction 5. Rhythm problems 6. Pericardial effusion	1. Tetralogy of Fallot 2. Double outlet RV. 3. Transposition of great arteries 4. Truncus arteriosus 5. Arch anomalies

Introduction

Pre-natal diagnosis of congenital heart disease (CHD) is accurately possible in the current era by fetal echocardiography [1]. Prenatal diagnosis permits family centered counseling about the prognosis and management options for the CHD before the baby is born. It also permits a holistic evaluation of the fetus with CHD including evaluation of the associated extra-cardiac and genetic anomalies. Further options of the pregnancy and neonatal care can be tailored according to the expected outcomes after treatment and in accordance to the family's preferences. It is imperative that prenatal diagnosis and counseling of major CHDs are undertaken sufficiently early in pregnancy so that all management options may be made available to the affected families. This is particularly true in countries like India with limited resources to manage complex congenital cardiac lesions needing multiple palliative procedures with guarded long-term outcomes.

Indications for Fetal Echocardiography:

Since most forms of congenital heart disease occurs in low-risk pregnancies, it is important to perform a basic screening of the fetal heart in all pregnancies. This should be done as a part of the mid trimester anomaly scan [2]. A combination of the four-chamber view, outflow tracts and three-vessel view enable accurate screening of the fetal heart [2,3]. In addition, a basic evaluation of the fetal heart rate and rhythm should be done in all pregnancies. Several protocols for the conduct of fetal heart evaluation has been published [4-6]; the ISUOG "extended basic protocol" including the situs, 4-chamber view, outflow tracts, 3 vessel and 3 vessel tracheal view enables detection of most significant forms of CHD [7]. In high-risk pregnancies (see Table I), screening of the fetal heart should begin early (11-14 weeks) and referral for a specialized fetal echocardiography may be considered at around 16-18 weeks [8,9]. Table I summarizes the recommended indications for fetal echocardiography. Figure 1 summarizes the common views for fetal heart screening.

Table I: Indications for Fetal Echocardiography

Fetal	Maternal	Familial
1. Abnormal 4 chamber view. 2. Extracardiac anomalies – GIT, spina bifida 3. Chromosomal anomalies - VACTERL, Trisomies, Digeorge 4. Increased first trimester NT 5. Non-immune hydrops 6. Irregular heart beat – tachy/ brady arrhythmias 7. Abnormal cardiac axis 8. IVF/ICSI	1. Maternal CHD 2. Teratogen exposure 3. Metabolic disorders – Diabetes Mellitus 4. Maternal auto-immune disease 5. Intra-uterine infections	1. Previous child with CHD 2. Paternal CHD 3. Mendelian syndromes – TS, Noonan's, Digeorge

Liver Diseases Complicating Pregnancy falls into Three General Categories[1]-

- Conditions specifically related to pregnancy and resolve either spontaneously or after delivery- Hyperemesis Gravidarum, acute fatty liver of pregnancy, intrahepatic cholestasis and HELPP Syndrome.
- Conditions coincidental to pregnancy- viral hepatitis
- Chronic liver diseases that predate pregnancy- chronic hepatitis, cirrhosis or oesophageal varices.

Pregnant women undergo certain physiological changes which can mimic liver disease. Hyper estrogenic state results in spider angioma and palmar erythema which are typical markers of liver disease. Decreased gall bladder motility increases incidence of cholelithiasis in pregnant women. Alkaline phosphatase (ALP) is increases during third trimester, rest all liver enzymes remain within the normal range during normal pregnancy. Clotting factors (I, II, V, VII, X, and XII) and fibrinogen levels are increased. Despite functional changes, there occurs no histological change in liver cells.

Viral Hepatitis

Viral hepatitis is caused mostly by 5 hepatotropic viruses, Hepatitis A, B, C, D and E.

Acute infections are mostly anicteric and often asymptomatic. The prodromal features of acute infections (nausea, vomiting, fever and malaise) precede jaundice by one or two weeks and symptoms subsides once jaundice occurs. The levels of serum transaminases vary with peaks not corresponding to disease severity. Almost all cases of hepatitis A, most of hepatitis B and few of hepatitis C cases, there is complete clinical and biochemical recovery in one to two months. But if there is intractable nausea and vomiting, central nervous system deterioration, prolonged prothrombin time, hypoglycaemia and high bilirubin levels, then hospitalisation with close monitoring is needed. Case fatality rate is 0.1% in acute hepatitis with mortality due to fulminant hepatic necrosis[1].

Chronic hepatitis infection is mostly due to hepatitis B and C virus infection.

Hepatitis A

Caused by RNA picornavirus, transmitted by faecal-oral route through ingestion of contaminated food or water. Infection is usually self-limiting but infected individuals continue to shed the virus in faeces and during the viremia period, their blood is also infectious. The incubation period is almost four weeks. Sign and symptoms are usually nonspecific with jaundice occurring in most. Presence of IgM anti HAV antibody confirms the diagnosis. There is no chronic state of hepatitis A.

Management during pregnancy mainly involves symptomatic support. There is no evidence that hepatitis A infection is teratogenic. Hepatitis A vaccination during pregnancy is recommended only in high risk adults. (ACOG 2012b, CDC 2010) Those recently exposed to HAV, passive immunisation is provided by 0.02 ml/kg immunoglobulin[1]. (Centres for Disease Control and prevention 2010)

Hepatitis B

Caused by double stranded DNA virus. It can be transmitted by exposure to any body fluid of an infected individual. The first virologic marker to appear in blood after infection with HBV is HBsAg. It typically disappears in 1-2 months after the onset of jaundice but rarely may persist beyond 6 months. So, when an asymptomatic pregnant lady comes out to be HBsAg positive, the main concern lies whether she is chronic carrier or has acute infection. Presence of HBeAg signifies high viral replication and correlates with detectable HBV DNA.

All pregnant women should be screened for hepatitis B virus (HBV) early in pregnancy or at the first visit itself. The risk of vertical transmission is minimal if the infection is acquired in first trimester. The risk is high, almost 60% to 90% if the infection is acquired during the third trimester or if mother is positive for the envelope antigen (eAg). Most of the neonates get infection during intrapartum period (95%) with intrauterine transmission being rare. A mother positive for both HBsAg and HBeAg has 70-90% risk of neonatal transmission whereas it is around 10-20% in only HBsAg positive cases[2,3]. Infants born to seropositive mothers should receive HBV immunoglobulin along with HBV vaccine. HBV immunoglobulin reduces transmission and prevents

infection in almost 90% cases if given within the first 24 hours of birth but it can still be given up to one week though efficacy is unknown. HBV vaccine can be given to high risk seronegative mothers, efficacy is similar to that of non-pregnant adults with overall 95% seroconversion rates[4].

Immunoprophylaxis failure occurs almost exclusively in cases with HBeAg-positive with high viral loads (HBV DNA levels >200 000 IU/mL) and/or HBsAg >4–4.5 log10 IU/ml. As per recent EASL recommendations, tenofovir disoproxil fumarate (TDF)is the first-line nucleoside analogues in pregnancy. Safety data is available for other nucleoside analogues also during pregnancy – lamivudine and telbivudine but TDF is preferred as it has a better resistance profile with more extensive safety data in pregnant HBV-positive women.[5-7]

HBV infection is not a contraindication for breast feeding but the safety of continuing drug treatment during pregnancy is unknown.

Hepatitis C

Caused by single stranded RNA virus. It is transmitted via blood and blood products, sexual contact and through needle sharing in intravenous drug users. Pregnancy is not known to modify the natural course of HCV disease. Huang et al. in their meta-analysis found that maternal HCV infection is significantly associated with an increased risk of preterm birth[8]. Vertical transmission via the mother's HCV RNA occurs in approximately 3–5% of cases.[9-10] The risk of transmission increases if there is associated HIV infection. Invasive procedures (e.g., amniocentesis, invasive fetal monitoring) should be avoided in infected mothers and their foetus to prevent vertical transmission of hepatitis C. Caesarean section is limited to obstetrical indications only and breast feeding is not contraindicated.

Hepatitis E

Caused by single stranded RNA virus, transmitted same as HAV. Mortality is almost 15-25% if mother acquires infection during the third trimester owing to fulminant hepatitis. Currently, there is no vaccine available for its prevention.

Hyperemesis Gravidarum

It is not a liver disease in true sense but it is associated with abnormal liver function tests in nearly 50% cases. Elevations in serum aminotransferases may rise up to 200 U/L. Treatment is supportive.

Intrahepatic Cholestasis of Pregnancy (ICP)

ICP is also known as recurrent jaundice of pregnancy, cholestatic hepatosis and icterus gravidarum is the most common pregnancy related liver disease with onset usually in the late second or third trimester of pregnancy. Risk factors include advancing maternal age, personal or family history of ICP, a history of cholestasis secondary to oral contraceptives, multiple pregnancy and fertility treatment. A higher prevalence is shown in patients with hepatitis C, cholelithiasis and non-alcohol fatty liver disease (NAFLD). It is characterised by abnormal liver function test which gets resolved after delivery.

Pathogenesis - Exact cause is unknown but a multifactorial etiology has been suggested involving genetic, hormonal and environmental factors. Genetic predisposition in ICP is viewed due to family clustering, presence of ethnic and geographic variations, and mutations in genes controlling hepatocellular transport systems. ICP occurs late in pregnancy and is more commonly seen in twin pregnancy, both of which has higher oestrogen levels and resolves after delivery, when levels of sex steroids decline, thereby suggesting hormonal involvement. Epidemiological data also suggests that ICP is more common during winter season. Mutation in the ABCB4 gene which encodes for the multidrug resistance protein 3 (MDR3) is implicated in some[11].

Whatever the cause may be, there is incomplete clearing of bile acids with accumulation in plasma. Hyperbilirubinemia resulting from retention of conjugated pigments seldom exceeds 5 mg/dl. Aminotransferases are usually increased by 2 to 10 times but seldom exceeds 250U/L. ALP is also raised, but this rise is non-specific due to placental production of the enzyme. Abdominal ultrasound shows no abnormal findings for the liver parenchyma and no dilatation of biliary ducts. Liver biopsy is characterized by intrahepatic cholestasis without parenchymal inflammation but it is rarely indicated.

Optimal Management Of Fetuses With Congenital Heart Defects: What An Obstetrician Should Know?

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12. Antenatal corticosteroids should not be administered if there is no substantiated clinical suspicion of preterm delivery in the next 2–7 days.

13. In women with symptoms of preterm labor, cervical length and fibronectin/PAMG1 measurements should be considered to prevent unnecessary hospitalization and use of tocolytic drugs and/or antenatal steroid.

These recommendations come as a welcome respite to numerous controversies and confusions in this subject. The choice of medication (Betamethasone or Dexamethasone) has been left to the individual doctor's discretion as there are no significant differences in the efficacy of one over the other. The exact salt available along with the ease of dosing can help in choosing the specific suitable medication.

Repeated doses are definitely not recommended but the options of a rationalised "rescue" dose remains. It may be noted that although separate evidence for multiple gestations is not extensive, the logical extrapolation of benefits from the evidence on singletons is expected and thus the use is accepted. These findings will change as new evidence and experience emerges and we will accordingly revise the information then.

Suggested Reading : FIGO Committee report. Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. FIGO Working Group on Good Clinical Practice in Maternal–Fetal Medicine. International Journal of Obstetrics and Gynecology . Volume144, Issue3 March 2019. Pages: 352-355 First Published:01 February 2019

Clinical Presentation - The most characteristic symptom is pruritus which shows predilection for the palm and soles and typically worsens at night. Jaundice is seen in only 14-25% cases, and may develop 1 to 4 weeks after the onset of pruritus[12,13].

Differential diagnosis includes other cholestatic conditions like primary biliary cirrhosis, primary sclerosing cholangitis, benign recurrent intrahepatic cholestasis, viral hepatitis and biliary obstruction.

Management -The first-line treatment for ICP is ursodeoxycholic acid (UDCA)given at a dose of 500 mg twice a day or 15 mg/kg per day. It has shown to relieve pruritus, lower bile acid and liver enzymes and improve neonatal outcome. Antihistamines and emollients may relief pruritus. Corticosteroids may be needed for fetal lung maturity depending on gestational age. Pregnancy should be terminated at 38 weeks of gestation. Caesarean section is done for obstetrical indications only.

Cholestasis and Pregnancy Outcomes - ICP has a high recurrence rate (60–70%) in subsequent pregnancies. It is a benign condition for mother with pruritus disappearing in the first two days following delivery. Biochemical parameters take weeks to months for resolution. Liver function tests and bile acid concentrations controls are recommended 6 to 8 weeks following delivery and if a woman has abnormal liver function tests for more than 3 months postpartum, she should undergo additional clinical investigations to exclude other or co-existing liver diseases. As compared to the favourable prognosis for women with ICP, there is poor perinatal outcome as there is increased risk of preterm labour, fetal distress, and sudden intrauterine fetal death. Elevated bile acids in circulation increase uterine contractions and fetal colonic muscle contractions thereby resulting in meconium staining. Bile acids after entering cardiomyocytes in abnormal amounts causes fetal death.[14]

Acute Fatty liver of Pregnancy- (AFLP, also known as Acute Fatty Metamorphosis or Acute Yellow Atrophy)

AFLP is a medical and obstetric emergency characterised by microvesicular fatty infiltration of hepatocytes. AFLP is a rare condition, usually occurring in the third trimester, with an approximate incidence of 1: 10,000 to 1: 15 000 pregnancies, maternal mortality being 18 %. It is more common in primiparous women older than 30 years, those with multiple gestations carrying a male foetus.

Pathogenesis - AFLP is associated with mitochondrial hepatopathy (similar to Reye's syndrome) and is attributed to a defect in mitochondrial beta oxidation of fatty acids. There is an association between AFLP and deficiency of the enzyme long chain 3 hydroxyacyl-CoA dehydrogenase (LCHA). Deficiency of this enzyme results in accumulation of long chain fatty acids in the liver. The most common mutation is G1528C and E474Q mutations of the gene on chromosome number 2 encoding for long chain 3 hydroxyacyl- CoA dehydrogenase[1].

Clinical Presentation and Laboratory Findings - Initial symptoms are nonspecific and include nausea, vomiting, and abdominal pain. Concomitant preeclampsia is present in roughly 50% of the affected women. These nonspecific manifestations should prompt vigilant monitoring as progression to jaundice, hypoglycaemia, disseminated intravascular coagulation encephalopathy, with frank liver failure can rapidly ensue resulting in poor maternal and fetal outcome. Serum bilirubin levels are < 10 mg/dl and serum aminotransferase levels are moderately elevated and usually less than 1000U/L.

Profound endothelial cell activation with capillary leakage results in haemoconcentration, acute renal injury, ascites and pulmonary oedema in almost all severe cases.[15]

Presumptive diagnosis of AFLP is based upon the presence of characteristic features (nausea, vomiting, abdominal pain, malaise, and/or anorexia) with significant hepatic dysfunction in second half of pregnancy, after excluding other causes.

The Swansea criteria includes symptoms, laboratory findings, and imaging, and is used for diagnosis of AFLP[16,17]. It includes the following-

- Vomiting
- Abdominal pain
- Polydipsia/polyuria
- Encephalopathy
- Elevated bilirubin (>0.8 mg/dL or >14 micromol/L)
- Hypoglycemia (<72 mg/dL or <4 mmol/L)
- Leukocytosis (>11,000 cells/microL)
- Elevated transaminases (AST or ALT)

(>42 international unit/L)
- Elevated ammonia (>47 micromol/L)
- Elevated uric acid (5.7 mg/dL or >340 micromol/L)
- Acute kidney injury, or creatinine 1.7 mg/dL or >150 micromol/L
- Coagulopathy or prothrombin time >14 seconds
- Ascites or bright liver on ultrasound scan
- Microvesicular steatosis on liver biopsy

Presence of 6 or more of these features in the absence of other aetiologies suggests AFLP[18].

Differential Diagnosis includes viral hepatitis and drug induced hepatitis. Presence of hypoglycaemia, prolongation of prothrombin time and absence of thrombocytopenia distinguishes it from HELPP syndrome.

Management - Early recognition and prompt delivery of the foetus is the mainstay of management. Caesarean section is usually the preferred mode of delivery to hasten hepatic healing though vaginal delivery may be attempted. As the mother is already in an energy deficient state owing to liver failure, putting her through the stress of vaginal delivery can worsen liver failure by straining the already depleted energy resources. Coagulopathy needs to be addressed prior to delivery with adequate blood product replacement. The syndrome continues to worsen after diagnosis but the good part is that delivery arrests liver function deterioration and hepatic dysfunction usually normalises within a week postpartum. The cause of maternal deaths are mainly sepsis, renal failure, haemorrhage, pancreatitis, and gastrointestinal bleeding.

HELLP Syndrome (Haemolysis, Elevated Liver Enzymes and Low Platelets)

HELLP syndrome is a severe form of pre-eclamptic liver dysfunction. Exact pathogenesis is not known but it is believed to be secondary to endothelial cell dysfunction and thrombotic microangiopathy. Diagnosis is based on presence of haemolysis (Serum lactate dehydrogenase > 600 U/L), elevated liver enzymes (serum aspartate aminotransferase > 70 U/L) and low platelets (<100 × 109/L).[18,19]

HELLP syndrome mostly presents in 3rd trimester, but nearly 1/4th of these patients can present in immediate post-partum period. Right upper quadrant abdominal pain, nausea and vomiting with or without jaundice are usual presenting symptoms. The symptoms usually revert after delivery but rarely there can be severe thrombocytopenia, septicaemia, disseminated intravascular coagulation and multi organ failure. The foetus is at risk of foetal growth restriction and iatrogenic prematurity but there is no risk of neonatal thrombocytopenia.

Management - Once diagnosis is made, women needs close monitoring with optimisation of blood pressure and seizure prophylaxis. Termination of pregnancy is the only definitive management. The decision to deliver the baby needs to be balanced considering gestational age. Immediate delivery is justified if it is near term (>34 weeks), evidence of foetal distress or when there are systemic complications such as disseminated intravascular coagulation, renal failure etc. Delivery can be delayed with careful monitoring in a small set of mild/ asymptomatic HELPP syndrome with steroids being given for fetal lung maturity[20]. Delivery is usually by Caesarean section but depends on case-to-case basis by the treating obstetrician.

Cirrhosis and Portal Hypertension

Pregnancy is relatively rare in decompensated cirrhosis. Cirrhotic pregnant women are at increased risk of transient hepatic failure, variceal bleeding, fetal growth restriction and preterm delivery[21].

Variceal bleeding is the most common and dreaded complication of portal hypertension during pregnancy. Risk is increased at delivery and during the second trimester owing to increased intravascular volume and compression from gravid uterus[22].

Each episode of variceal bleeding increases maternal mortality rates as 20–50% associated with increased fetal loss[23].

Treatment of acute variceal bleeding during pregnancy should be focused on resuscitation and hemodynamic stabilization of the mother along with endoscopic control of variceal bleeders. Octreotide is category B drug and can be used as an adjunct therapy in acute variceal bleeding along with antibiotics. Trans jugular intrahepatic portosystemic stent shunting (TIPSS) is an interventional radiology procedure used to control bleeding unresponsive to other measures[24].

Another dreaded complication of cirrhosis is rupture of associated splenic artery aneurysms[21].

The outlook for preterm outcomes changed dramatically over the last century with the advent of antenatal corticosteroids that helped in accelerating fetal lung maturity primarily and in preventing some other neonatal complications too. The drastic reduction in perinatal morbidity and mortality in the premature neonatal cohort has been rightfully credited to these medications. However, there is still a great deal of confusion about how and how not to use these potential steroids. The correct preparation, dosage and route remains a bit enigmatic to the general clinicians because practices keep changing based on current recommendations and there is a need for constant updating of knowledge in this regard. This article has summarised the basic practice points as per the most recent recommendations by peer reviewed academic processes. There still remain some grey zones – especially regarding “limits of viability” . There will be considerable controversy and discrepancy if a uniform definition were to be adopted by all but while there is hardly any doubt about justified use after 26 weeks gestation – the period from 24-26 weeks remains a grey zone. Hence the most rational approach is to follow your “local limits” in accordance with the supporting neonatal team.

FIGO working group on good clinical practice in Maternal–Fetal medicine (2015-2018) in its latest report on antenatal corticosteroids recommends the following:

1. Clinicians should offer a single course of prenatal corticosteroids to all women between 24 and 34 weeks of gestation who are at risk of preterm birth within 7 days.

2. Administration of corticosteroids for pregnant women at less than 24 weeks of gestation with a risk of preterm birth within 7 days is linked to a family’s decision regarding resuscitation. Due consideration should be given to local limits of fetal viability when determining the lowest limit of gestational age at which steroids should be administered.

3. A single course of betamethasone is recommended for pregnant women between 34 and 36.6 weeks of gestation with a risk of preterm birth within 7 days, and who have not received a previous course of antenatal corticosteroids. Although there is a paucity of data on longer-term follow-up.

4. A single course of corticosteroids can be considered for women undergoing planned cesarean delivery at 37–38.6 week’s gestation. However, there should be a clear medical reason; an elective delivery should not be performed before 39 week’s gestation.

5. The most extensively studied regimens of corticosteroids treatment for the prevention of RDS are: two doses of betamethasone 12 mg given intramuscularly 24 hours apart, or four doses of dexamethasone 6 mg given intramuscularly 12 hours apart.

6. Antenatal corticosteroids are most effective in reducing RDS in pregnancies that deliver 24 hours after and up to 7 days after administration of the second dose of antenatal corticosteroids.

7. Weekly repeat courses of antenatal corticosteroids are not recommended.

8. A single repeat course of antenatal corticosteroids should be considered in women at less than 34 weeks of gestation who have an imminent risk of preterm delivery within the next 7 days, and whose prior course of antenatal corticosteroids was administered more than 7–14 days previously.

9. One course of antenatal corticosteroids should be administered to all patients who are between 24 and 34 weeks of gestation and at risk of delivery within 7 days, irrespective of whether a single or multiple birth is anticipated.

10. Antenatal corticosteroid therapy is recommended for women with pre-gestational and gestational diabetes who are at risk of imminent preterm birth. Women who are receiving fetal steroids should have additional insulin according to an agreed protocol and be closely monitored.

11. There is insufficient evidence to conclude on the benefits or harms of antenatal corticosteroids therapy in women whose infants are growth restriction.

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Rational Use Of Antenatal Corticosteroids In Current Practice

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Pregnancy with Liver Transplantation

Fertility is restored in most women with a liver transplant just after one year. The main concern in this category of patients is that they are on lifelong immunosuppressive drugs. Close surveillance is needed to detect preeclampsia and graft rejection.

Westerbrook et al audited all liver transplant patients with pregnancy and reported that 117 conceptions occurred in 79 patients with median age of conception of 29 years. Graft loss (2%), acute cellular rejection (ACR; 15%), pre-eclampsia/eclampsia (15%), gestational diabetes (7%), and bacterial sepsis (5%) were the maternal adverse effects. ACR was significantly higher in women who conceived within 12 months of transplant (P = 0.001). The live birth rate was 73%. No significant effect on pregnancy outcomes and complications was seen with the choice of immunosuppressive drugs (cyclosporine versus tacrolimus)[25].

Key Points-

- Liver disease during pregnancy may pose a serious threat to the mother.
- They may be related or unrelated to pregnancy. Physiological changes must be kept in mind.
- Most common cause of jaundice during pregnancy is viral hepatitis, most severe being hepatitis E infection during pregnancy with mortality rates being 15-25%.
- All pregnant women should be screened for hepatitis B antigen at the first visit itself.
- Most common pregnancy related liver disease is cholestasis of pregnancy with onset usually in the late second or third trimester of pregnancy. Pregnancy must be terminated at 38 weeks of gestation.
- Fatty liver is an obstetrical and medical emergency needing multidisciplinary approach.
- Variceal bleeding is a dreaded complication of portal hypertension during pregnancy requiring endoscopic control of variceal bleeders.

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Multiple pregnancies are seen more common nowadays due to advancing maternal age and frequent use of assisted reproduction. There is a higher risk of almost every potential complication of pregnancy in women with multi-fetal pregnancy. Apart from prematurity which is the most grave problem, other reasons for adverse perinatal outcome are an increased potential for congenital anomalies and fetal growth restriction, including certain unique complications such as twin-twin transfusion syndrome (TTTS) seen in monochorionic twins. As a consequence, antenatal care and perinatal management for women with multiple pregnancies has become more challenging.

Planning of Delivery and Management of Labor:

Delivery planning for a multi-fetal pregnancy involves a careful consideration of the delivery setting with facility of caesarean section, apt and adequate healthcare staff including obstetrician, paediatrician and anaesthesia facilities.The decision is of timing delivery usually triggered by smaller twin, in case of selective intrauterine fetal growth restriction (sFGR),however there is a risk of iatrogenic prematurity for normally grown co-twin. Thus, any adverse outcome is generally shared by both twin pair.

Planning of delivery includes a clear strategy for:

1. Route of delivery
2. Timing of delivery

Management of labor is almost similar to singleton pregnancy with some differences, as intrapartum management of a muti-fetal pregnancy can pose various challenges for the obstetrician. This involves continuous fetal heart rate monitoring of both fetuses and carefully conducting the delivery as there is a significant amount of risk at the time delivery especially for the after coming fetus which may be due to malpresentation or cord prolapse.[1] Thus, it should be discussed with emphasis on following :

1. General preparation for labor and delivery
2. Rational use of drugs used for induction/ augmentation of labor and labour analgesia
3. Electronic fetal heart monitoring
4. Intrapartum management and general principles of conducting a twin delivery by a skilled obstetrician well versed in external cephalic version (ECV)and/ or internal podalic version (IPV)
5. Management of third stage of labor

Route of Delivery :

It should be individualised for each patient as the choice depends on factors such as amnionicity, presentation of first fetus, period of gestation, discordancy between fetuses, other comorbidities and availability of 24 hour services for caesarean section.

Diamniotic twins with presenting twin in cephalic presentation can reasonably undergo vaginal delivery regardless of the presentation of the second fetus, provided there is adequate intrapartum monitoring, the obstretrician can conduct breech extraction if required and 24 hours facility for caesarean section is available.[2] However, diamniotic twins with non-cephalic presenting twin should preferably be delivered by caesarean section. Monoamniotic twins should be delivered by cesarean section in order to avoid risk due to cord entanglement in labor. It is noted that there is an increased incidence of adverse outcome when weight of the 2nd twin is >20% or if there is a discordancy of >40%, hence, caesarean section is preferred route of delivery in such patients also.[3] Also, cesarean delivery is the most favourable route of delivery for triplet gestations. In addition, caesarean delivery is also recommended route of delivery for any standard obstetric indications as in singleton pregnancies. In cases of patients with previous one caesarean, the decision for route of delivery is not very conclusive. As there is uncertainity about the safety of planned vaginal birth after caesarean (VBAC) in twin gestation, a cautious approach is advised by RCOG if VBAC is planned for such patients.[4] However, ACOG states that trial of labor after caesarean (TOLAC) can be considered in women with one previous caesarean with a low transverse incision, who are otherwise suitable candidates for twin vaginal delivery.[2]

1. Timing of Delivery

Chorionicity and amnionicity are important factors that determine the time of delivery in uncomplicated multi-fetal pregnancies. The optimal timing is truly based on each clinical picture and earlier delivery may be indicated after individualization in complicated pregnancies.

Uncomplicated Twins:

- **Dichorionic/ Diamniotic:** The American college of Obstetricians (ACOG) and Society of Maternal Fetal Medicine (SMFM) recommends deliveryat 38 to 38+6 weeks. However, The Royal College

administration of even the first dose of betamethasone/ dexamethasone has been found to be useful in decreasing the neonatal morbidity and mortality. No additional benefit is obtained by giving accelerated dosing of steroids (in a shorter dosage interval). Benefits of corticosteroids are greatest at 2-7 days after initial dose.

Role of Rescue Dose of Corticosteroids

ACOG suggests that a single repeat course of antenatal corticosteroids should, be considered in women who are less than 34 weeks of gestation, who are at risk of preterm delivery within the next 7 days, and whose prior course of antenatal corticosteroids was administered more than 14 days previously. Rescue course corticosteroids could be provided as early as 7 days from the prior dose, if indicated by the clinical scenario [(18-19)]. Whether to administer a repeat or rescue course of corticosteroids with preterm premature rupture of membranes is controversial, and there is insufficient evidence to make a recommendation for or against.

Role of Magnesium Sulphate

Multiple observational studies, clinical trials and randomized trials have shown the beneficial effect of pre-delivery administration of magnesium sulphate with neuroprotective intent to decrease the risk of neonatal intracranial hemorrhage and cerebral palsy prior to 32 weeks of gestation. Magnesium acts in many intracellular processes, and its actions include cerebral vasodilation, reduction in inflammatory cytokines and/ or oxygen free radicals, and/or inhibition of calcium influx into cells [(20-21)]. It should be administered to all patients with preterm labour when birth is anticipated between 24 weeks and 33+6 weeks of gestation. While most guidelines suggest that the inclusion criteria, treatment regimens, concurrent tocolysis, and monitoring should be tailored according to the hospital policies, the most studied and suggested dose is 4gm in 100ml NS over 30min followed by 1gm/hr infusion until birth or for 24 hours whichever is earlier. If the clinical scenario doesn't permit the completion of the entire maintenance dose due to imminent delivery, at least the loading dose of 4gm should be given for utmost benefit.

Role of Antibiotics

Intrauterine bacterial infection is an important cause of preterm labour, especially at gestational ages less than 32 weeks [(21)]. It has been theorized that infection or inflammation is associated with contractions. Hence, traditionally antibiotics have been empirically given for the treatment of infection if any. However clinical studies have not found any advantage of antibiotics in prolonging pregnancy, preventing preterm delivery, reducing respiratory distress syndrome, neonatal sepsis and improving the neonatal outcome after administration of antibiotics in the absence of any intrauterine infection. However, in the setting of preterm premature rupture of membranes and Group B streptococci carrier status, antibiotic administration has been advocated to reduce the risk of chorioamnionitis for both the mother and the baby. The use of amoxicillin and clavulanic acid is not recommended for women with preterm premature rupture of membranes because of the increase risk of necrotizing enterocolitis with amoxyclav compared to erythromycin. Oral erythromycin 200 mg four times a day for 10 days is recommended.

Role of Non-Pharmacological Measures

Non-pharmacological measures like bed rest, hydration, sedation and abstinence from sexual activity have not been found to be useful in prevention or management of preterm labour. Potential harm of prolonged bed rest maybe venous thromboembolism, bone demineralization and loss of employment.
Optimal mode of birth for women in preterm labour
Routine delivery by caesarean section instead of vaginal delivery, for the purpose of improving preterm new-born outcome, is not recommended regardless of fetal presentation. Caesarean section should only be performed for obstetric indications.

To Summarise

- Not all patients who come with spontaneous preterm labour deliver prematurely.
- Clinical examination is necessary to establish the diagnosis of preterm
- Transvaginal USG / Fetal fibronectin may be useful to determine those at high chance of delivery within 48 hours and requiring tocolysis
- Tocolytics are given only for 48 hours to buy time for steroid action, magnesium sulphate and in utero transfer
- No long-term maintenance tocolysis
- Nifedipine and atosiban have comparable effectiveness
- Beta-agonists have a high frequency of adverse effects. Not recommended
- A single course of corticosteroids is recommended for pregnant women between 24 and 34 weeks of gestations who are at risk of delivery within 7 days
- Magnesium sulphate should be given to women with established preterm labour for neuroprotection
- No routine antibiotics in preterm labour

TABLE 1: Target Non-Myometrial Tissues Where Tocolytics Act and Produce Side Effects

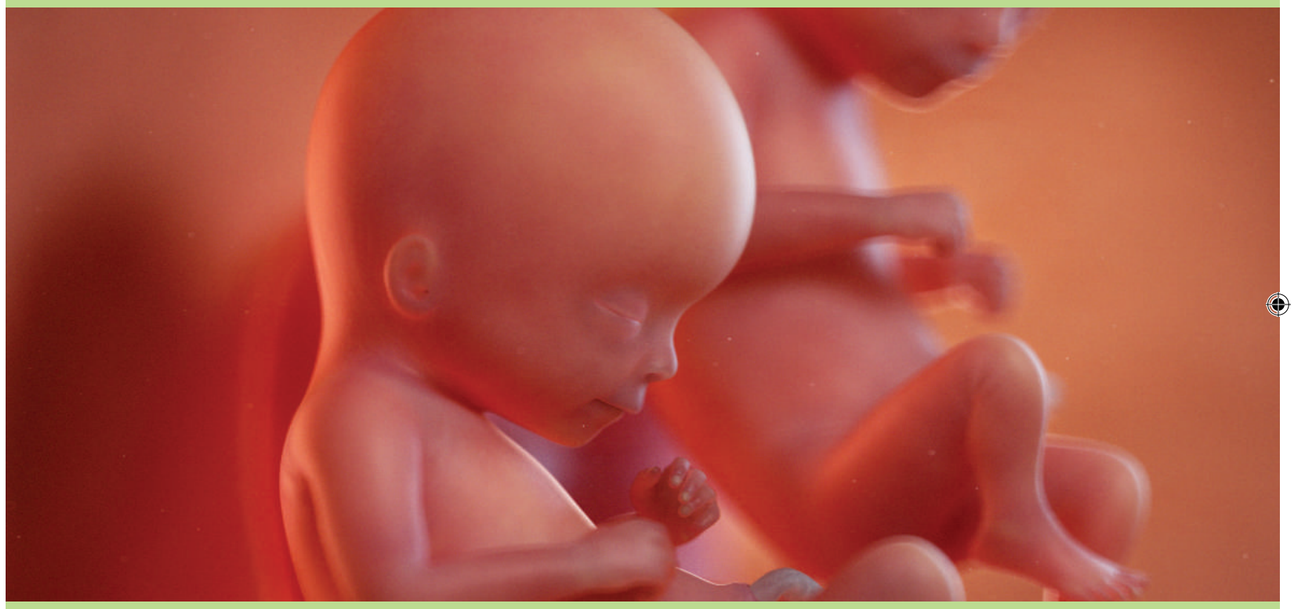
Agent	Non-myometrial Tissues Responsive
ß-adrenergic receptor agonists	Myocardium, Smooth muscles, Juxtaglomerular cells, Skeletal muscle, Liver
Calcium channel blockers	Vascular smooth muscle, Cardiac conduction
Magnesium sulphate	Smooth muscle, Brain receptor, Neuromuscular junction blockage
Nitric oxide donors	Vascular smooth muscle

TABLE 2: Side Effects and Contraindications to Tocolytics

Agent or Class	Maternal side effects	Fetal or New-born adverse effects	Contraindications
Calcium channel blockers	Dizziness, flushing, hypotension, decrease in heart rate, contractility and LV systolic pressure, increase in liver enzymes	None	Hypotension and pre-load dependent cardiac lesions like aortic stenosis
Nonsteroidal anti-inflammatory drugs	Nausea, esophageal reflux, gastritis, vomiting, breathlessness, chest discomfort, pulmonary edema, hypocalcemia, hypergylcemia	Intrauterine Constriction of ductus arteriosus, oligohydramnios, necrotising enterocolitis in preterm new-borns,	Platelet dysfunction, bleeding disorders, liver dysfunction, peptic ulcers, renal dysfunction, asthma
Beta adrenergic receptor agonists	Tachycardia, hypotension, tremors, palpitations, breathlessness, chest discomfort, pulmonary edema, hypocalcemia, hypergylcemia	Fetal tachycardia	Tachycardia sensitive maternal heart disease, uncontrolled diabetes
Magnesium sulphate	Flushing, diaphoresis, nausea, loss of deep tendon reflexes, respiratory depression, cardiac arrest	Neonatal depression	Myasthenia gravis

Figure 1: Transabdominal USG assessment of cervical length with partly full bladder
Figure 2: Transvaginal USG assessment of cervical length with empty bladder
Figure 3: Y shaped funnelled cervix
Figure 4a,b: U shaped funnelled cervix with bulging membranes on transvaginal and transabdominal USG
Figure 5: Cerclage as seen on transvaginal USG

Perinatal Management Of Multi-Fetal Pregnancy



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these drugs are greater than the risks associated with preterm birth.

- Intrauterine fetal demise
- Lethal fetal anomaly
- Nonreassuring fetal status
- Severe preeclampsia or eclampsia
- Maternal bleeding with haemodynamic instability
- Chorioamnionitis
- Preterm premature rupture of membranes
- Maternal contraindication to tocolysis

Tocolytics are given only to delay delivery for 48 hours,

- To allow ante partum glucocorticoids to induce lung maturation &
- Magnesium sulphate for neuroprotection
- In utero transfer to a tertiary care centre with NICU facilities.

After control of the acute symptoms and signs of preterm labour (uterine contractions being the most important), maintenance therapy with tocolytics is ineffective for preventing preterm birth and improving neonatal outcomes and is not recommended for this purpose. Short term prolongation of pregnancy afforded by tocolytics does not actually translate into statistically significant neonatal benefit [15].

Spectrum of Tocolytic Agents (tokos: childbirth, lytic: capable of dissolving)

- ß-mimetics
- MgSO4
- Nitric Oxide donors
- Cyclo-oxygenase inhibitors
- Ca Channel Blockers
- Oxytocin antagonist

The primary target of tocolytics is the myometrial cell. However, most tocolytics act on non-myometrial tissues also. The wide distribution of responsive tissue is major determinant of numerous undesired side effects with these agents (Table1).

Is one tocolytic drug more effective in preventing preterm birth than another? (Table 2)

- Nifedipine is first line tocolytic which is offered to women between 26 to 33+6 weeks who are in suspected or diagnosed preterm labour
- Nifedipine and atosiban have comparable effectiveness in delaying birth for up to seven days. If nifedipine is contraindicated, offer oxytocin receptor antagonist for tocolysis
- Compared with beta-agonists, nifedipine is associated with improvement in neonatal outcome
- Calcium channel Blockers/ Nifedipine has the advantages of oral administration and a low purchase price.
- Beta-agonists have a high frequency of adverse effects.
- Magnesium sulphate is associated with adverse effects and is ineffective in delaying preterm birth.

Nifedipine

Initial oral dose of 20 mg followed by 10–20 mg three to four times daily, adjusted according to uterine activity for up to 48 hours. A total dose above 60 mg appears to be associated with a three- to four-fold increase in adverse events.

Atosiban

A suggested dose of atosiban of an initial bolus dose of 6.75 mg over 1 minute, followed by an infusion of 18 mg/hour for 3 hours, then 6 mg/hour for up to 45 hours (to a maximum of 330 mg).

Role of Antenatal Corticosteroids

Antenatal corticosteroids are the only pharmacotherapeutic option for management of preterm labour that has been found to be beneficial in improving neonatal outcome. Antenatal corticosteroids significantly lower the severity, frequency, or both of respiratory distress syndrome, intracranial hemorrhage, necrotizing enterocolitis and death thus improving neonatal morbidity and mortality [16].

ACOG recommends a single course of corticosteroids for pregnant women between 24 weeks and 34 weeks of gestation who are at risk of delivery within 7 days, irrespective of membrane status or singleton/ multifetal gestation. A single course of corticosteroids may also be considered starting at 23 weeks of gestation depending on the family's decision for resuscitation. Also, betamethasone has been found to useful to decrease risk of respiratory distress syndrome in late preterm gestation i.e. between 34 to 36+6 weeks at risk of delivery within 7 days and who haven't received corticosteroids previously.

The corticosteroids approved for use include betamethasone and dexamethasone. Treatment, for either a primary or a rescue course, should consist of either two 12-mg doses of betamethasone given intramuscularly 24 hours apart or four 6-mg doses of dexamethasone every 12 hours administered intramuscularly [17]. If the clinical scenario doesn't permit completion of the above-mentioned courses,

of Obstetricians (RCOG) recommend that delivery between 37 to 38 weeks is optimum.[5]

- **Monochorionic/Diamniotic:** The American College of Obstetricians (ACOG) and Society of Maternal Fetal Medicine (SMFM) recommends delivery between 34+0 to 37+6 weeks of gestation.However, a planned delivery at 36+0 to 37 weeks is recommended by RCOG.[5]

- **Monochorionic/ Monoamniotic:** Plan delivery between 32+0 and 34+0 weeks of gestation regardless of intensive fetal monitoring due to very high risk of stillbirth.

Complicated Monochorionic Twins:

- Delivery of monochorionic twin pregnancies complicated by TTTS and treated with laser photocoagulation of anastamotic vessels should be between 34+0 and 36+6 weeks of gestation (should be individualized).[6]

- In type I sFGR (refer table 1 below), delivery should be considered by 34–36 weeks of gestation provided there is satisfactory fetal growth velocity and normal umbilical artery Doppler waveforms.[6]

- In type II and III sGR (refer table 1 below), delivery should be considered by 32 weeks of gestation, unless significantly abnormal velocity of fetal growth or worsening of the fetal Doppler assessment.[6]

Table 1:
Classification of sFGR in Monochorionic Twins

S.No	Type of sFGR	Doppler changes in umbilical artery of the smaller twin
1	I	Positive end-diastolic pattern
2	II	Persistent absent or reversed end diastolic pattern
3	III	Intermittent absent or reversed end diastolic pattern

In monochorionic twins very preterm delivery may be required if the twins are viable and one of them is compromised and there is risk of impending fetal death. If one twin dies in utero there is risk of neurological damage or death of normal twin, this is due to vascular communications between the twins.

Complicated Dichorionic Twins:

Management of Dichorionic twins is not as challenging because each fetus has its own placenta with no intervening vascular communications. They behave as singletons conceptually and the pattern of the growth-restricted twin almost follows like a single fetus with growth restriction. Thus, in case of growth restriction of one fetus, it is preferable to time the delivery in such a way that the risk of morbidity for the appropriately grown twin is negligible. Therefore, in contrast to complicated monochorionic twins,in case of fetal compromise and impending death in one twin , it may be wise to allow death of one fetus rather than subject the normal fetus to risk of extreme prematurity.

Triplets: (Based on Amnionicity)

Monoamniotic or diamniotic triplets – Plan delivery at32+0 to 32+6 weeks of gestation

Triamniotic triplets – Plan delivery at 35+0 and 35+6 weeks of gestation.

2. General Preparation

At the time of admission for delivery, an intravenous access should be established and blood should be sent for cross-matching. Adequate blood and blood products should be arranged as there is a high risk of atonic post-partum haemorrhage during delivery. Inform neonatologist, one for each baby are required at the time of delivery and also anaesthetist.

3. Rational Use of Drugs for Induction/ Augmentation of Labor and Analgesia

Induction of Labour:

The safety profile of cervical ripening agents and the approach to their use is similar as in singleton pregnancies.[7,8]

Augmentation of Labour:

Oxytocin can be used safely and the regimen for its use in singleton pregnancies is found to be as effective in twins also.[9]

Analgesia:
Epidural analgesia is suitable for pain relief and can also be useful if internal podalic version or caesarean delivery is required.[10]

4. Fetal Heart Rate Monitoring

Fetal heart needs to be monitored intensively and continuously due to a higher chance of intrapartum complications in multifetal gestation. As there might be difficulty to differentiate fetal heart of one twin from the other, intermittent auscultation is not a very practical approach for monitoring. A single machine with double-channel outflow can be used for electronic fetal heart rate monitoring of both the fetuses. This is especially useful for monitoring of fetal heart rate of the second twin during the delivery also, high-risk period after delivery of the first twin.

5. General Principles in Conducting a Twin Delivery

Intrapartum fetal monitoring should continue. The procedure for delivery of the presenting cephalic fetus is the same as in singleton delivery, including indications for episiotomy and operative vaginal deliveries. After the delivery of the first twin, the cord should be clamped and marked for proper identification. However, the protocol for delayed cord clamping differs slightly in twins. Due to risk of acute inter-twin blood transfusion with unpredictable direction of flow, it is not suitable to perform delayed cord clamping in monochorionic twins. However, the practice of delayed cord clamping is safely recommended in dichorionic twins.[11]
Following delivery of first twin, the obstetric care provider should perform a rapid clinical abdominal and vaginal examination to assess the lie, presentation and fetal heart of the second twin which can be supplemented by ultrasound evaluation and electronic fetal heart monitoring. Continuous fetal heart monitoring should be done for the second twin. Traditionally, a period of 30 minutes was considered safe interval between delivery of first and second twin but on subsequent evaluation it was observed that there does not have to be a finite interval between delivery as long as the fetal heart is reassuring and vigilant monitoring for fetal heart rate is done.[12,13]

Second Twin with Cephalic Presentation:
contractions should be monitored and sometimes oxytocin augmentation of labor is needed in case adequate contractions are not established.[14] Artificial rupture of membranes is generally performed during a contraction when the head is engaged.

Second Twin with Non-Cephalic Presentation:

- **a) Oblique or transverse lie:** External version to longitudinal lie can be performed under continuous fetal heart monitoring. If it is unsuccessful and oblique or transverse lie persist, internal podalic version with breech extraction may be attempted under anesthesia. In case of lack of expertise for the above, caesarean section may be done instead.
- **b) Footling Breech:** Delivery may be attempted by breech extraction if obstetrician is skilled, otherwise caesarean section may be done.

Unplanned cesarean delivery can occur for the delivery of the second twin in case of malpresentation, cord proplapse, abnormal fetal heart rate pattern and /or maternal complications.[15]

6. Management of Third Stage of Labor

Overdistention of the uterus due to multifetal pregnancy predisposes to atonic post-partum haemorrhage. However, the active management of the third stage of labor does not differ in these when compared to singleton pregnancies, uterotonics should be given after delivery of second baby in twins. A careful assessment of blood loss should be done in all cases.

Key Points:

1. Multiple gestation is a high risk pregnancy seen increasingly nowadays and their surveillance protocol and timing of delivery should be planned properly as per recommendations.
2. The delivery of twins must be planned at a facility with 24 hour operation theatre facilities, blood bank facility and a skilled obstetrician in manoeuvres such as IPV and breech extraction.
3. Vaginal delivery is the preferred mode of delivery for twins with first twin in cephalic presentation in the absence of standard indications for cesarean delivery
4. Cesarean is preferred mode of delivery in case of first twin with non-cephalic presentation, monoamniotic twins, triplets and higher order pregnancies, in case of monochorionic twins with a discordancy of 40% or second twin weight >20% of the first and standard obstetric indications for caesarean delivery
5. Intrapartum fetal heart monitoring should be done carefully with continuous cardiotocography of both twins

Screening for risk of preterm birth in women with current singleton pregnancy without history of preterm.
ACOG does not mandate universal cervical length screening in women without a prior preterm but this screening strategy may be considered. If a second trimester transabdominal malformation scan suggests that the cervix may be short or may have some other abnormality, it is recommended that a transvaginal USG be performed to better visualise the cervix and establish its length.
Management of women who do not have a history of preterm birth but who are found to have a short cervical length
Vaginal progesterone is recommended as a management option to reduce the risk of preterm birth in asymptomatic women with a singleton gestation without a prior preterm birth with an incidentally identified short cervical length less than or equal to 25mm before or at 24 weeks of gestation. For women in otherwise low risk population, cerclage placement in women with a cervical length less than 25mm detected between 16 weeks of gestation and 24 weeks of gestation has been associated with a significant reduction in preterm birth at less than 35 weeks of gestation.

Consider prophylactic cervical cerclage for women with a transvaginal ultrasound done between 16-24 weeks and a cervical length less than 25 mm and who have either a preterm premature rupture of membranes in previous pregnancy or a history of cervical trauma.

Preterm Labour Management

Less than 10% of women with clinical diagnosis of preterm labour deliver within 7 days. About 30% of preterm labour spontaneously resolve. Almost 50% of patients hospitalized for preterm labor give birth at term.

Tests to be used to stratify risk for preterm delivery in patients who present with preterm contractions
Transvaginal ultrasound and fetal fibronectin may help health care providers reduce unnecessary resources. Positive predictive value of a positive fetal fibronectin test or short cervical length alone is poor.

Cervical length measurement
If the clinical assessment suggests that the women is in suspected preterm labour consider transvaginal ultrasound measurement of cervical length to determine likelihood of birth within 48 hours. If the cervical length is more than 15 mm the patient is unlikely to be in preterm labour. If the cervical length is 15 mm or less, the patient is in diagnosed preterm labour and must be treated with tocolytics.

Fetal fibronectin testing
Fetal fibronectin testing is indicated as a diagnostic test to determine likelihood of birth within 48 hours if cervical length assessment is not available.
While FFN has a LR of 3 for predicting preterm birth in low risk asymptomatic women, its value of FFN probably lies in its high negative predictive value (>95%). This means that a negative FFN (concentration 50 ng/ml or less) virtually rules out preterm labor risk and can reduce admissions and intervention. If fetal fibronectin testing is positive (concentration > 50ng/ml) the woman should be diagnosed as preterm labour and offered treatment.

However, FFN cannot be performed with:

- Vaginal bleeding
- Ruptured membranes
- After recent intercourse
- After vaginal examination
- After transvaginal ultrasound

Traditionally many pharmacological and non-pharmacological treatments have been advocated for management of preterm labour. However, most of the non-pharmacological treatments like bed rest, abstention from intercourse and orgasm, sedation and hydration have very little evidence of their effectiveness, while adverse effects have been reported [11–14].
The pharmacological treatments include tocolytics, antibiotics, antenatal corticosteroids and magnesium sulphate. Out of these only antenatal corticosteroids for fetal lungs maturity and magnesium sulphate for fetal neuroprotection have been clearly associated with improved neonatal outcomes.

Indications for treatment in Preterm Labor

- Women with preterm contractions without cervical change should not be treated with tocolytics.
- Tocolytics are not indicated for use before neonatal viability
- The upper limit for the use of tocolytic agents is 34 weeks

Contraindication to tocolysis: Tocolysis is contraindicated when the maternal and fetal risks of prolonging pregnancy or the risks associated with

angiogenesis and tendency for inflammation), elevated levels of interleukin-1ß (IL-1ß) have been found to be associated with preterm delivery[10].

Maternal Serum Markers

Maternal serum calponin[1] and ratio of maternal serum alpha fetoprotein (AFP)/amniotic fluid AFP have been suggested as a potential predictor for preterm delivery.

Newer Tools: Combination of anterior cervical angle, cervical length, and maternal characteristics, measurement of utero-cervical angle (between lower uterine segment and cervical canal) (>95 degrees and >105 degrees detected in second trimester may indicate increased risk for PTB <37 and <34 weeks respectively), uterine artery pulsatility index during peak of uterine contraction in women with threatened PTL, Placental strain ratio, central zone of fetal adrenal gland measurement, lower fetal MCA PI, assessment of cervical consistency including cervical strain elastography and shear wave elastography[10].
For prediction of PTB, FIGO (2019) recommends strategies as follows; proper identification of symptomatic patients in true PTL, taking into consideration of new risk factors (fetal male sex, stress, previous LSCS, ART etc), combined use of cervicometry and biochemical markers for improved detection of imminent spontaneous PTB, fetal fibronectin testing for its good negative predictive value, use of transvaginal ultrasound to measure cervical length in symptomatic patients (cervical length less than 15mm to identify patients at risk and more than 30mm to exclude the risk), tests based on PAMG-1; Partosure with highest NPV and PPV in patients with CL between 15 and 30mm, judicious use of antenatal steroids by adequate PTB risk assessment[10].

Priority Intervention

1. Preventing preterm birth
2. Management of preterm labour and delivery
3. Care of a premature baby

Primary Prevention Of Preterm Birth

Preconception health care for the prevention of preterm birth for all women

- Prevent pregnancy in adolescence
- Prevent unintended pregnancies and promote birth spacing practices
- Optimize pre-pregnancy weight
- Promote healthy nutrition including micronutrient supplementation
- Promote vaccination of children and adolescent
- Smoking cessation

Preconception health care for the prevention of preterm birth for women with special risk factors that increase the probability of preterm birth.

- Prevent and treat sexually transmitted infections including HIV
- Promote cessation of smoking and tobacco chewing
- Screen for, diagnose and manage preconception any chronic maternal disease like diabetes and hypertension

Secondary prevention of preterm labour for women with risk factors for preterm birth

- Cervical cerclage
- Antibiotics
- Progesterone

Protocol for Management of At Risk Patient

Management of current pregnancy in a woman with prior spontaneous preterm delivery

A woman with a singleton gestation and a prior spontaneous preterm singleton birth should be offered progestrone supplementation starting at 16-24 weeks of gestation to reduce the risk of recurrent spontaneous preterm birth.

In women with a current singleton pregnancy, prior spontaneous preterm birth at less than 34 weeks of gestation and short cervical length (less than 25 mm) before 24 weeks of gestation, cerclage placement is associated with significant decreases in preterm birth and offers perinatal benefits. Cerclage may be considered in women with combination of history & ultrasound findings.

Offer a choice of either vaginal progesterone or cervical cerclage for women with a history of spontaneous preterm birth or midtrimester loss between 16-34 weeks and a transvaginal USG shows a cervical length less than 25 weeks between 16-24 weeks (FIGURE 5)

No evidence to support the addition of an alternative form of progesterone if a short cervix is identified in a woman with a prior preterm birth who is already receiving preventive progesterone therapy.

There is no evidence to suggest that switching from treatment with intramuscular progesterone to vaginal progesterone is beneficial if a short cervix is identified

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Fetal Growth Restriction: Review Of New Concepts

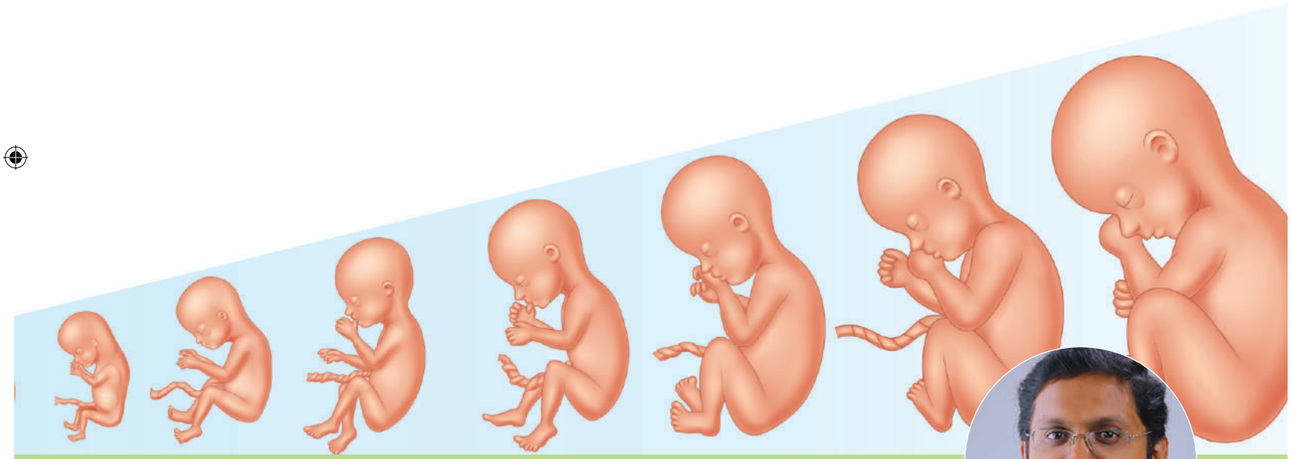

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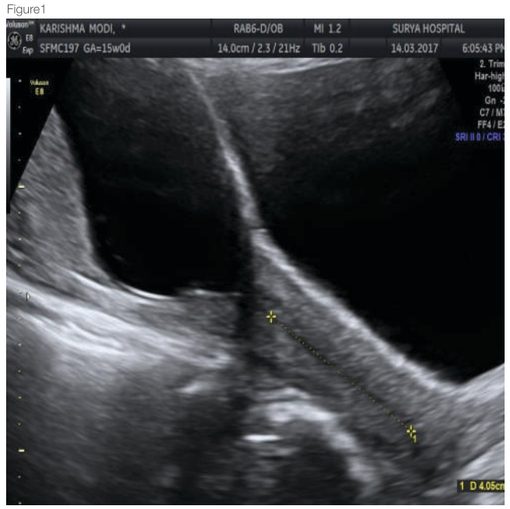
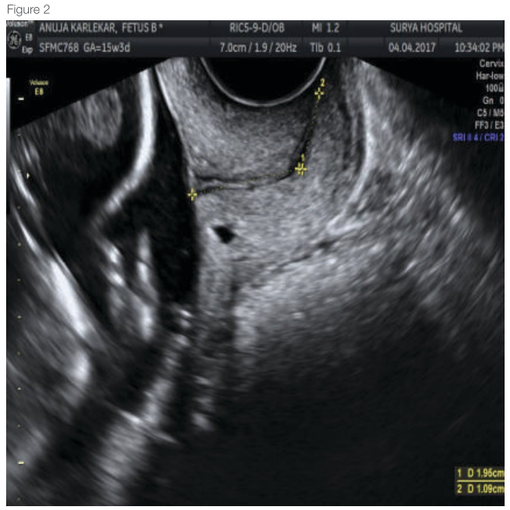
Figure1



The transvaginal probe is placed in the anterior fornix of the vagina with an empty maternal bladder avoiding undue pressure on the cervix. A faint line of echo density between internal and external os is measured using callipers placed at the internal and external os. For assessment of cervical dynamic shortening, measurements should be made over approximately 5 min. Fundal pressure may be applied to rule out presence of dynamic shortening. Presence of funnelling of internal os and or amniotic fluid sludge may also be noted. The shortest of three cervical length measurements is taken[8].

Figure 2



Short cervical length on TVS commonly defined as <25mm (10th centile) before 24 weeks, has been found to be associated with increased risk of PTB[9].

(FIGURE 3,4a,b) However, routine TVS screening at a single point time in the general antenatal population is not recommended because of poor positive predictive value of short CL in low risk. There is conflicting evidence on screening of cervical length in first trimester[9].

Figure 3

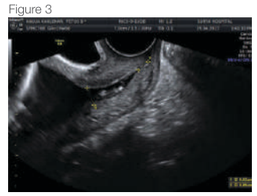


Figure 4a

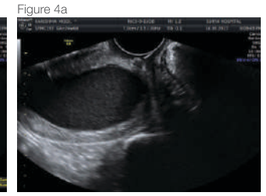


Figure 4b

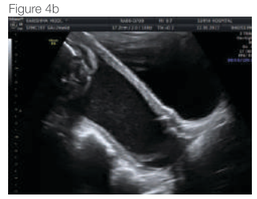
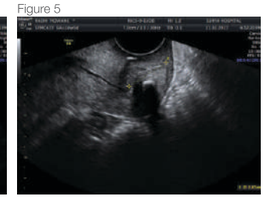


Figure 5



Biochemical Markers and Other Modalities

Fetal fibronectin screening, bacterial vaginosis testing, home uterine activity monitoring etc have been proposed to predict PTB. However, studies have failed to demonstrate an improved outcome after interventions based on these tests. Therefore, these methods are not recommended for screening[7,9,10.]

Cervical Fluid Markers:

Fetal fibronectin: Fetal fibronectin is a glycoprotein produced by amniocytes and cytotrophoblasts that binds chorio-amniotic membranes to maternal decidua. It is normally found in cervicovaginal fluids before 22 weeks of gestation but its presence in cervicovaginal fluid between 24 and 34 weeks of gestation indicates a risk for preterm birth. It is most accurate in predicting preterm birth in women with threatened preterm labour without advanced cervical dilatation within 7-10 days after testing[7,9].

IL-6 and IL-8 levels, Placental alpha macroglobulin-1 (PAMG-1) assessed by a bedside test PartoSure, Insulin-like growth factor binding protein-1 (IGFBP-1) are found to be present at significantly higher rates in cervical fluids of patients with PTB.[10]

Amniotic Fluid Based Tests:

Low amniotic fluid glucose, increased vascular endothelial growth factor (VEGF), placental growth factor (PGF), and decreased soluble VEGF receptor-1 (sFlt-1) at 16–19 weeks of gestation (indicating

1. BEHAVIORAL AND PSYCHOLOGICAL Excessive alcohol consumption, smoking, cocaine abuse, unfavourable diet, prolonged and stressful physical activities in antenatal period, short inter-conception interval (<6 months).

2. SOCIODEMOGRAPHIC AND COMMUNITY RELATED Extremes of maternal age (<17 or >35 years), unmarried status, poverty, adverse neighbourhood, lower educational level, racial disparity (African-American have higher PTB rates)

3. PREVIOUS PRETERM BIRTH (one of the strongest predictors)

4. SHORT CERVIX (cervical length <25mm at 24 weeks on TVS in singleton pregnancy increases the risk by six-fold). Shorter the cervical length greater is the risk Cervical funnelling may add to preterm risk. History of cervical surgery including conization , LEEP, trachelectomy increases risk. Uterine instrumentation including multiple dilatation and curettage / hysteroscopy/ 2nd trimester terminations are cervical factors. Obstetric trauma like cervical laceration during previous delivery may also be a risk factor.

5. GENETIC FACTORS (Positive family history of PTB)

6. INFECTIONS (overt or subclinical intrauterine infections, vaginal infection e.g. Bacterial vaginosis, periodontal disease, urinary tract infections, malaria)

7. MULTIFETAL GESTATION (due to uterine overdistension, or indicated PTB due to maternal or fetal complications.

8. PREGNANCIES AFTER ART (Multifetal/singleton gestation following ART at two-fold higher risk)

9. MATERNAL BODY HABITUS (UNDERWEIGHT OR OBESITY) (low pre-pregnancy BMI< 19.8 increases risk by 1.5-2.5-fold whereas obesity is not associated with increased risk but leads to other complications which may result in indicated PTB.

10. MEDICAL AND OBSTETRIC CONDITIONS (Chronic hypertension, hypertensive disorders of pregnancy, SLE, pregestational DM, cardiac disease, asthma, renal disorders, and GDM, Placental previa, abruption, first trimester vaginal bleeding, uterine malformations)

Prediction of Preterm Birth

Although it is difficult to predict the events which lead to PTB and the associated PPROM, but various risk scoring systems, biochemical and ultrasound markers e.g. cervical length have been proposed to identify women at risk. Prediction of PTB is of utmost importance as it allows clinicians to transfer fetus in-utero to higher centre for better neonatal intensive care services.

Among all the above-mentioned risk factors only previous history of preterm birth and short cervix in current pregnancy are the two most important risk factors for preterm birth. Current predictive tests can be divided into three categories: assessment of risk factors, cervical ultrasound based cervical length measurement, and biochemical markers [7].

Assessment of Clinical Risk Factors

Prior preterm birth is one of the strongest risk factors which increases the risk by 1.5 to 2-fold. Recurrence risk is significantly affected by number of prior PTBs and gestational age at delivery. There is a 40% recurrence if previous preterm birth occurred before 30 weeks.

Current pregnancy events such as vaginal bleeding in first trimester, UTIs including untreated asymptomatic bacteriuria, lower genital tract infections, periodontal disease etc may also increase the risk. Behavioural risk factors like low pre-pregnancy BMI, smoking, substance abuse, short inter-conception period also increase the risk[7].

Transvaginal Cervical Ultrasonography

Transvaginal ultrasound assessment is the ideal investigation to estimate cervical length. It is safe, reliable and reproducible. TVS for cervical imaging is found to be superior to digital examination and transabdominal sonography, which tend to overestimate the cervical length with poor inter-observer reproducibility and reliability[8]. TVS is not affected by obesity or a full or empty bladder or shadowing by the pubic symphysis as in a transabdominal ultrasound. (FIGURE 1, 2)

Introduction

Intrauterine growth restriction (IUGR) is a common and complex obstetric problem. IUGR is noted to affect approximately 10-15 % of pregnant women [1]. The study of the natural history of IUGR or fetal growth restriction (FGR) has particular challenges. First, growth failure is often not detected antenatally, and in routine clinical practice, as many as three-quarters of babies at risk of IUGR are not recognized as such before delivery[2]. In low-risk pregnancy, with a lower threshold of suspicion, the detection rate is even lower, about 15%[3]. Second, when IUGR is recognized, the pregnancy is likely to be interrupted if the growth failure is considered severe and if the babies are mature enough to have a better chance ex utero. Therefore, most qualitative and quantitative evidence for the significance of IUGR comes from the retrospective assessment of the birthweight of live or stillborn babies.

Definitions

Small-for-gestational age for a fetus in utero is an estimated fetal weight that measures < 10th percentile on ultrasound. This diagnosis does not necessarily imply pathologic growth abnormalities, and may simply describe a fetus at the lower end of the normal range[4]. Intrauterine growth restriction refers to a fetus with an estimated fetal weight <10th percentile on ultrasound that, because of a pathologic process, has not attained its biologically determined growth potential[4].

Brief Description of Methods and Indices for Fetal Assessment

Fetal well-being tests and indices could be classified as chronic or acute. The former become progressively abnormal due to increasing hypoxemia and/or hypoxia, the latter correlate with acute changes occurring in advanced stages of fetal compromise, characterized by severe hypoxia and metabolic acidosis, and usually precedes fetal death in a few days.

In general, FGR is associated with Doppler signs suggesting hemodynamic redistribution as a reflection of fetal adaptation to undernutrition/ hypoxia, histological and biochemical signs of placental disease[5].

Umbilical Artery Doppler

UA Doppler is the only measure that provides both diagnostic and prognostic information for the management of FGR. It is used for diagnosis of FGR, alone or combined in the CPR ratio. The progression of UA Doppler patterns to absent or reverse end-diastolic flow correlates with the risks of injury or death. Up to 40% of fetuses with acidosis show this umbilical flow pattern [6] . There is an association between reversed end-diastolic flow in the UA and adverse perinatal outcome (with a sensitivity and specificity of about 60%)[7] . It cannot be solely used for diagnosis of Late onset FGR as the degree of placental disease in Late FGR is mild, thus UA Doppler is normal in virtually all cases [8].

Middle Cerebral Artery Doppler

MCA informs about the existence of brain vasodilation, a surrogate marker of hypoxia. MCA is considered a late manifestation, with acceptable specificity but low sensitivity. There is an association between abnormal MCA PI and adverse perinatal and neurological outcome, but it is unclear whether delivering before term could add any benefit. MCA is particularly valuable for the identification and prediction of adverse outcome among late-onset FGR, independently of the UA Doppler, which is often normal in these fetuses [8].

Cerebroplacental Ratio

The CPR is essentially a diagnostic index. The CPR improves remarkably the sensitivity of UA and MCA alone, because increased placental impedance (UA) is often combined with reduced cerebral resistance (MCA). Thus, the CPR is already decreased when its individual components suffer mild changes but are still within normal ranges [9] . An abnormal CPR predicts neurobehavioral problems at 18 months of age [10] . Interestingly, the anterior cerebral artery CPR rather than the MCA-CPR showed the stronger association.

Ductus Venosus Doppler

DV is the strongest single Doppler parameter to predict the short-term risk of fetal death in early-onset FGR. Longitudinal studies have demonstrated that DV flow waveforms become abnormal only in advanced stages of fetal compromise [11]. Absent or reversed velocities during atrial contraction are associated with perinatal mortality independently of the gestational age at delivery , with a risk ranging from 40 to 100% in early-onset FGR [12]. In about 50% of cases, abnormal DV precedes the loss of short-term variability (STV) in computerized cardiotocography (cCTG), and in about 90% of cases it is abnormal 48–72h before the biophysical profile (BPP) [13]. Hence, it is considered to provide a better window of opportunity for delivering fetuses in critical conditions at very early gestational

ages after completion of steroids.

Aortic Isthmus Doppler

The aortic isthmus (AoI) Doppler is associated with increased fetal mortality and neurological morbidity in early-onset FGR [14] . This vessel reflects the balance between the impedance of the brain and systemic vascular systems [15]. AoI has a strong association with both adverse perinatal and neurological outcome [14]. However, longitudinal studies show that the AoI precedes DV abnormalities by 1 week. Reverse AoI could already be incorporated in clinical protocols as a sign of severe placental insufficiency and could justify considering elective delivery beyond 34 weeks of gestation.

Cardiotocography

CTG has a 50% rate of false positives for the prediction of adverse outcome . In addition, a meta-analysis on high-risk pregnancies failed to demonstrate any beneficial effect in reducing perinatal mortality. Hence, there is no evidence to support the use of traditional fetal heart rate (FHR) monitoring or 'nonstress tests' in FGR foetuses[16]. Current evidence suggests that cCTG is sensitive to detect advanced fetal deterioration, and it provides a value similar to DV reverse atrial flow for the short-term prediction of fetal death. STV closely correlates with acidosis and severe hypoxia and can be used as an acute marker [11].

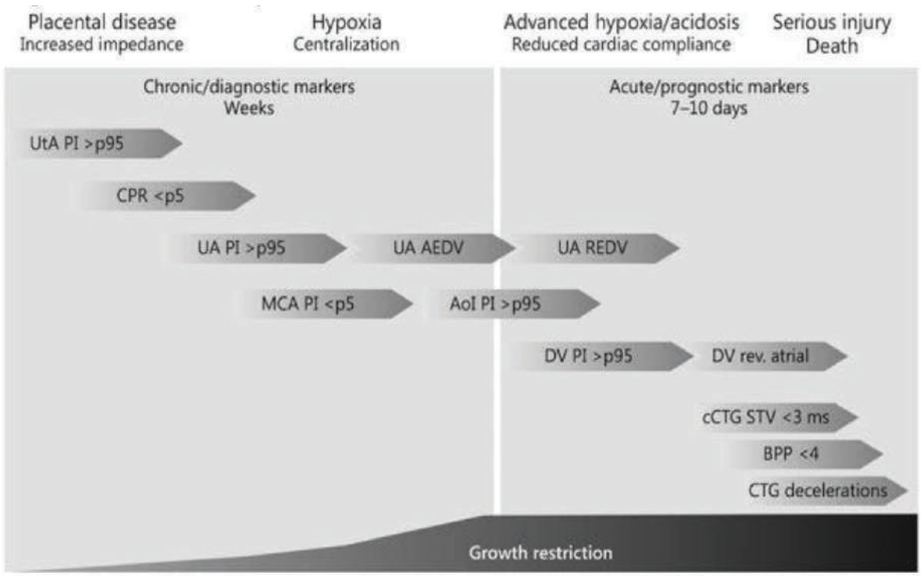
Classification

In a first step, once a small fetus (i.e. EFW <10th centile) has been identified, UtA PI, UA PI, MCA PI and the CPR should be measured in order to classify FGR versus SGA. When either CPR, UtA PI or EFW <p3 is abnormal, the risk of adverse perinatal outcome is increased. Thus, the definition of FGR should include these three parameters[5].

Early-Onset Fetal Growth Restriction

Early-onset FGR represents 20–30% of all FGRs [17]. Early-onset FGR is highly associated with severe placental insufficiency and with chronic fetal hypoxia. This explains that UA Doppler is abnormal in a high proportion of cases [18] . it often follows a cascade of changes which are reflected in a pattern of Doppler changes that allows to monitor the progression of fetal deterioration and tailor elective delivery (fig.1). Management is challenging and aims at achieving the best balance between the risks of leaving the fetus in utero versus the complications of prematurity.

Sequence of Events in Early-Onset FGR



Background

On December 25, 1642 when a widow gave birth prematurely to a male child, his mother Hannah Ayscough described that child as "so small that he could have been put into a quart mug" (≈ 1.3 litres)." The infant survived and grew up to be "Sir Isaac Newton." However, fact is that a significant proportion of preterm births do not survive, let alone grow to become Newton.

Definitions

As per WHO, babies who are born alive before 37 completed weeks of gestation (<366/7 weeks/ less than 259 days), are defined as Preterm [1]. Those born before 336/7are early preterm and those born between 34 and 36 completed weeks are late preterm. Diagnosis of preterm labour is based on clinical criteria of regular uterine contractions, accompanied with change in cervical dilatation, effacement or both.

Burden of Preterm Birth and Its Complications

An estimated 15 million babies are born preterm every year. Approximately, 12% of all live births occur before term. In India, out of 27 million babies born every year, 3.5 million babies born are premature[2]. More than 60% of preterm births occur in Africa and South Asia. According to recent statistics on preterm birth (as per WHO, 2018), India has been ranked first with greatest number of preterm births (3,519,100) followed by China (1,172,300)[3]. Preterm infants are particularly vulnerable to complications due to impaired respiration, difficulty in feeding, poor body temperature regulation and high risk of infection. Preterm birth is the most common cause of new born deaths worldwide, and the second leading cause of all child deaths under five, after pneumonia[3]. Preterm births, especially those <32 weeks of gestation, are at highest risk of neonatal death along with ongoing post-neonatal mortality risk, significant risk of long-term neurodevelopmental impairment (cerebral palsy, learning disabilities), and growth failure/ stunting, and adult-onset noncommunicable diseases, leading to physical, emotional and economical stress to family and health systems of all countries[4].

Preterm birth rates have remained the same over the years in spite of better obstetric management probably due to the increase in multiple pregnancies from ART and iatrogenic deliveries. Current evidence suggests that more than three-fourth of preterm deaths are preventable.

"Survive and thrive" report published in 2019 by WHO and UNICEF, focuses upon transforming care for every small and sick new-borns (who are the most vulnerable targets for death and disability) by strengthening care of babies born too small (<2500g) or too soon (<37weeks) in all countries through increased investment, round the clock neonatal care and better partnership with families[5].

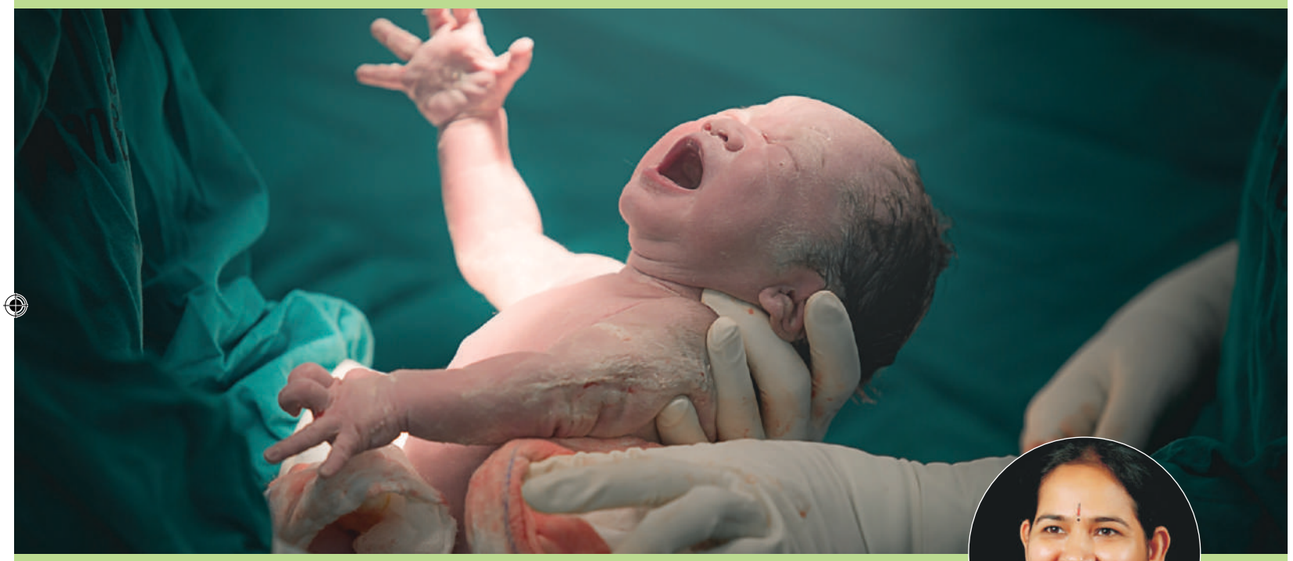
WHO guidelines published in 2015 focuses upon interventions during pregnancy, labour and neonatal period with the aim to improve outcomes in premature infants. The 10 main recommendations include antenatal corticosteroids, tocolytics for inhibiting preterm labour, magnesium sulphate for fetal neuroprotection against neurological complications, antibiotic prophylaxis in PPROM/ preterm labour, optimal mode of preterm delivery for mother, thermal care for preterm neonates by providing kangaroo mother care, radiant warmers, incubators or wrapping in plastic bags, continuous positive airway pressure for new-borns with RDS, surfactant administration for new-borns with RDS and oxygen therapy and concentration for preterm newborns[6].

Etiology And Risk Factors

Majority of PTBs occur due to preterm labour and other causes include PPROM, hypertensive disorders of pregnancy, FGR, cervical incompetence, intervention for maternal or fetal problems, and antepartum haemorrhage. PTBs can be classified as spontaneous PTB(results after spontaneous onset of PTL or PROM before the onset of labour, accounting for up to 60% of all PTBs) and indicated PTB (accounts for about 40% of all PTBs, occurs after medical intervention in order to reduce adverse perinatal outcomes in presence of specific medical/ surgical or obstetric indication for maternal or fetal interest)[4,7].

Exact cause for the onset of PTL is still not known. However, various risk factors have been found to be associated with this condition. The main etiology of spontaneous PTB is thought to be ascending infection from lower genital tract invading the decidua, chorioamniotic membranes, amniotic fluid and fetus in few cases. Infection results in an inflammatory reaction which triggers myometrial contractions, PPROM, and cervical ripening, leading to PTB[4].

Optimising Outcome In Preterm Births- Predicting, Preventing, And Managing Preterm Births Optimally



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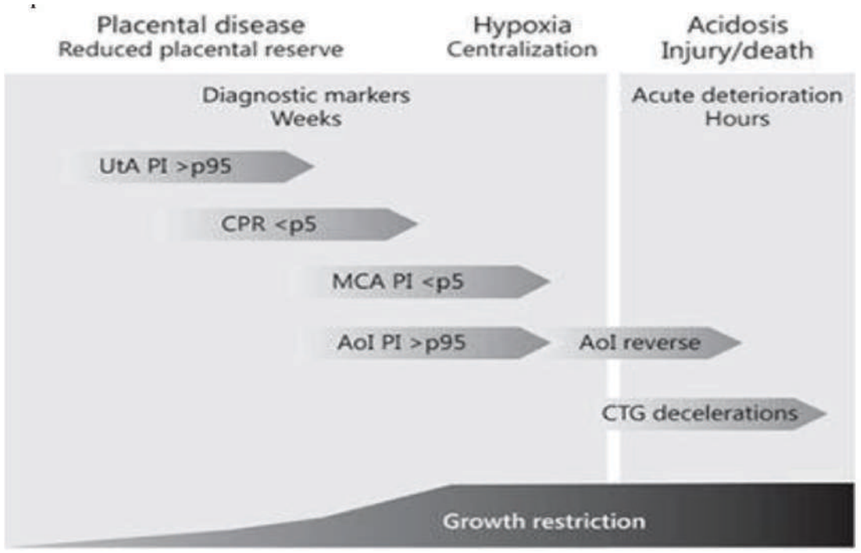
Late-Onset Fetal Growth Restriction

Late-onset FGR represents 70–80% of FGR [17] . The degree of placental disease is mild, thus UA Doppler is normal in virtually all cases [8] . There is a high association with abnormal CPR values [8] . In addition, advanced brain vasodilation suggesting chronic hypoxia, as reflected by an MCA PI <p5, may occur in 25% of late FGR [8] . Advanced signs of fetal deterioration with changes in the DV are virtually never observed [8] . Thus, the cascade of sequential fetal deterioration described above does not occur in late FGR. Late FGR lacks a 'natural history' and may undergo rapid deterioration leading to severe injury or death without observable late-stage signs as in early FGR (Fig. 2).

Sequence of Events in Late-Onset FGR



Summary of the Main Differences Between Early- and Late-Onset Forms of FGR

Early-Onset FGR (1 – 2%)	Late-Onset FGR (3 – 5%)
Problem: Management	Problem: Diagnosis
Placental Disease: Severe	Placental Disease: Mild
Hypoxia ++: Systemic Cardiovascular Adaptation	Hypoxia +/–: Central Cardiovascular Adaptation
Immature Fetus = Higher Tolerance to Hypoxia = Natural History	Mature Fetus = Lower Tolerance to Hypoxia = No (or very short) Natural History

Stage-based classification and management of FGR Small-for-Gestational Age.
EFW<10percentile, all dopplers are normal:- Fortnightly doppler and growth assessment is required. Labor induction should be recommended at 40 weeks[5].

Stage I Fetal Growth Restriction (Severe Smallness or Mild Placental Insufficiency).
Either UtA, UA or MCA Doppler, or the CPR are abnormal. In the absence of other abnormalities. Weekly monitoring seems reasonable. Labor induction beyond 37 weeks is acceptable, but the risk of intrapartum fetal distress is increased [5].

Stage II Fetal Growth Restriction (Severe Placental Insufficiency).
This stage is defined by UA absent-end diastolic velocity (AEDV) or reverse AoI. Monitoring twice a week is recommended. Delivery should be recommended after 34 weeks[5].

Stage III Fetal Growth Restriction (Advanced Fetal Deterioration, Low-Suspicion Signs of Fetal Acidosis). The stage is defined by reverse absent end diastolic velocity (REDV) or DV PI >95th centile. Monitoring every 24–48h is recommended. Delivery should be recommended by cesarean section after 30 weeks[5].

Stage IV Fetal Growth Restriction (High Suspicion of Fetal Acidosis and High Risk of Fetal Death).
This stage is defined by spontaneous FHR decelerations, reduced STV (<3 ms) in the cCTG, or reverse atrial flow in the DV Doppler. Monitoring every 12–24h until delivery is recommended. Deliver after 26 weeks by cesarean section at a tertiary care center under steroid treatment for lung maturation[5].

Table 2. Stage-Based Classification and Management of FGR

Stage	Pathophysiological Correlate	Criteria (Any of)	Monitoring*	GA/Mode of delivery
I	Severe smallness or mild placental insufficiency	EFW <3rd centile CPR <p5 UA PI >p95 MCA PI <p5 UtA PI >p95	Weekly	37 weeks LI
II	Severe placental insufficiency	UA AEDV Reverse AoI	Biweekly	34 weeks CS
III	Low-suspicion fetal acidosis	UA REDV DV-PI >p95	1-2 days	30 weeks CS
IV	High-suspicion fetal acidosis	DV reverse a flow cCTG <3ms FHR deccelerations	12 h	26 weeks** CS

All Doppler signs described above should be confirmed at least twice, ideally at least 12 h apart. GA = Gestational age; LI = Labor induction; CS - Cesarean section.
*Recommended intervals in the absence of severe preeclampsia. If FGR is accompanied by this complication, strict fetal monitoring is warranted regardless of the stage.
**Lower GA threshold recommended according to current literature figures reporting at least 50% intact survival. Threshold could be tailored according to parents' wishes or adjusted according to local statistics of intact survival.

Note at early gestational ages, and at whatever stage, coexistence of severe PE may distort the natural history and strict fetal monitoring is warranted since fetal deterioration may occur unexpectedly at any time[5].

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