HIGH RISK PREGNANCY & CRITICAL CARE OBSTETRICS

Department of Medical, Health and Family Welfare

Government of Uttar Pradesh

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MESSAGE

SHRI BRIJESH PATHAK

Hon'ble Deputy Chief Minister
Minister of Medical Health and
Family Welfare Department
Government of Uttar Prades

Continuing Medical Education (CME) offers medical professionals an opportunity to expand their knowledge base and allows experts to share their expertise with the wider medical community. CMEs promote collaboration among healthcare professionals, creating valuable networking prospects.

In pursuit of sustainable development goals and to alleviate the global burden of non-communicable diseases, the Government of Uttar Pradesh is dedicated to enhancing its Healthcare Ecosystem through CME, integrating technological advancements and medical breakthroughs.

Primary Health Centers (PHCs) and Community Health Centers (CHCs) serve as the first point of contact with qualified doctors in the public health sector. By implementing structured CME programs, these initiatives aim to upgrade the skills and knowledge of medical officers, thereby significantly improving patient care, fostering patient confidence, and increasing patient satisfaction.

Aligned with this objective, the State Institute of Health & Family Welfare, Uttar Pradesh (SIHFW), is actively creating CME modules crucial for our healthcare personnel. I believe that the High Risk Pregnancy and Critical Care Obstetrics module, emphasizing recent advancements, will greatly enhance the expertise of medical officers in the Provincial Health & Medical Services in Uttar Pradesh. This will ultimately benefit both the medical officers and their patients.

I offer my best wishes to the SIHFW team in their ongoing development of CME modules, which will undoubtedly be advantageous for the medical officers in the Provincial Health & Medical Services in Uttar Pradesh, subsequently enhancing the well-being of their patients.

(Brijesh Pathak)


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MESSAGE

Shri Mayankeshwar Sharan Singh

Hon'ble State Minister
Medical Health and Family
Welfare Department
Government of Uttar Pradesh

I take great pride in the fact that the State Institute of Health & Family Welfare, Uttar Pradesh (SIHFW), is addressing the critical need for knowledge enhancement among Medical Officers in the Provincial Health & Medical Services in Uttar Pradesh through its Continuing Medical Education (CME) module focused on High Risk Pregnancy and Critical Care Obstetrics.

Given the constant advancements in medical science and research, it is imperative for doctors to remain updated on current practices and trends. There is a widespread recognition that CME programs are essential to systematically impart recent knowledge and skills, thereby enhancing the existing proficiency of medical professionals.

This module aims to consolidate pertinent information in the domains of high risk pregnancy and critical care obstetrics, encompassing screening, detection, referrals, and patient treatment. It is designed to serve as a practical resource that can be periodically reviewed and updated based on the experiences gained from implementing public health services.

In light of these efforts, SIHFW has developed a CME module specifically focused on critical care obstetrics treatment for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh. I hope that this CME module is just the beginning of a series of initiatives that will assist our Medical Officers in staying current with intervention practices.

I extend my best wishes to the director and the dedicated team at the State Institute of Health & Family Welfare (SIHFW) in Lucknow, Uttar Pradesh, in their mission to contribute to an improved healthcare delivery system through Continuing Medical Education, especially in the areas of Critical Care Obstetrics.

(Mayankeshwar Sharan Singh)


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FOREWARD

Shri Partha Sarthi Sen Sharma

Principal Secretary
Department of Medical, Health
and Family Welfare
Government of Uttar Pradesh

The Continuing Medical Education (CME) module serves as a means for medical professionals to stay updated on the rapidly evolving practices within the field of medicine. Given the ongoing COVID era, it has become increasingly crucial for medical officers to stay abreast of emerging modes of treatment and management, which are developed based on feedback from the medical community.

Medical officers at the primary level face numerous challenges in managing critical care obstetrics. Continuous improvement in knowledge and skills is essential to effectively address these challenges. However, due to their responsibilities in overseeing healthcare centers and implementing government policies, medical officers have limited time available for learning.

To tackle and rectify this situation, the State Institute of Health & Family Welfare (SIHFW) in Uttar Pradesh has designed a specialized CME module focusing on Critical Care Obstetrics for Medical Officers in the Provincial Health & Medical Services. This module has been developed in collaboration with experts in the field.

The module offers a comprehensive overview of recent advancements in screening, prevention, and advanced treatment for high risk pregnancy and critical care obstetrics. Its primary objective is to enhance the expertise and knowledge of Medical Officers, ultimately leading to an enhancement in healthcare services for the general population.

I want to extend my congratulations to SIHFW and the other subject matter experts who played a role in crafting this comprehensive module. I am optimistic that this CME module will shed light on the treatment of High Risk Pregnancy and Critical Care Obstetrics, contributing to improved healthcare outcomes.

(Partha Sarthi Sen Sharma)


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MESSAGE

Dr. Deepa Tyagi
Director General
Medical and Health Services
Uttar Pradesh

The effective management of High Risk Pregnancy and Critical Care Obstetrics is pivotal in preserving lives and preventing serious health complications. Swift access to well-equipped healthcare facilities capable of handling medical emergencies is crucial for saving lives and minimizing physical impairments.

To meet the specific needs of Medical Officers in the Provincial Health & Medical Services of Uttar Pradesh, the State Institute of Health & Family Welfare (SIHFW) has designed an extensive Continuing Medical Education (CME) program centered on High Risk Pregnancy and Critical Care Obstetrics. This program encompasses the latest advancements in the field and offers detailed guidance on essential management approaches for these conditions at the primary level. The objective is to facilitate early screening, detection, referrals, and treatment of patients.

Upon completion of this CME program, it is anticipated that Medical Officers in Uttar Pradesh will be able to elevate their service delivery through proficient screening, effective case management, appropriate referrals, and provision of treatment within their healthcare facilities. Consequently, communities will enjoy enhanced access to healthcare services, heightened patient satisfaction, and improved overall population health. This CME program not only enriches clinical and technical proficiency but also reinforces the delivery of healthcare services, bridging the gap between theoretical knowledge and practical application in healthcare management.

We extend our warmest wishes to the SIHFW team and look forward to the release of many more customized CME modules in the times ahead.

(Dr. Deepa Tyagi)


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MESSAGE

Dr. Brijesh Rathor
Director General Family Welfare,
Directorate of Family Welfare
Uttar Pradesh

Continuing Medical Education (CME) modules provide a means for healthcare professionals to stay abreast of the swiftly evolving practices in the field of obstetrics. Particularly in the realm of the High Risk Pregnancy and Critical Care Obstetrics module, it has become increasingly essential for medical officers to stay updated on treatment methods and management approaches.

Medical officers operating at the primary healthcare level encounter numerous challenges in effectively handling cases involving critical care obstetrics. Ongoing acquisition of knowledge and skills is imperative to tackle these challenges. However, due to their responsibilities in managing healthcare facilities and implementing government policies, medical officers have limited time for further education and skill development.

To address and rectify this situation, the State Institute of Health & Family Welfare (SIHFW) in Uttar Pradesh has formulated a specialized CME module centered on the treatment of High Risk Pregnancy and Critical Care Obstetrics for Medical Officers in the Provincial Health & Medical Services in Uttar Pradesh. This module incorporates the most recent advancements in the treatment of High Risk Pregnancy and Critical Care Obstetrics patients. Its primary objective is to enhance the expertise and knowledge of Medical Officers, leading to an improvement in healthcare services for the population.

I want to extend my congratulations to SIHFW and the subject matter experts who played a role in creating this comprehensive module. I am hopeful that this CME module will shed light on the effective treatment of High Risk Pregnancy and Critical Care Obstetrics.

(Dr. Brijesh Rathor)


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MESSAGE

Dr. Shailesh Kumar Shrivastava

Director General (Training)
Medical Health and Family Welfare
Uttar Pradesh

High Risk Pregnancy and Critical Care Obstetrics treatment is very important in saving lives and serious obstetrics conditions. The reaching of an effected women to a center which has facilities for treatment of obstetrics helps in saving lives and physical impairment.

This module on Continuing Medical Education (CME) on High Risk Pregnancy and Critical Care Obstetrics treatment for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh provides a coherent and research-based insight to obstetrics Management. It has been designed and written for Medical Officers and healthcare professionals and takes government perspective in consideration, drawing upon and comparing ideas and developments from national and international health care practices.

I hope that after this CME, Medical Officers in Uttar Pradesh will be able to scale up the services delivery in provide screening, management, referral and treatment in critical care obstetrics, thus benefitting communities. In addition to improving clinical and technical area of expertise, this CME will lead to providing improved access to obstetrics services and enhancing patient satisfaction and population health.

The director and the team at State Institute of Health & Family Welfare, Uttar Pradesh and the team of experts of the field has done a commendable job by publishing this CME module on High Risk Pregnancy and Critical Care Obstetrics for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh. I hope the participants coming to attend their upcoming CME will take advantage of this initiative and make the most in their field with this handy module.

(Dr. Shailesh Kumar Shrivastava)


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ACKNOWLEDGEMENT

Dr. Rajaganapathy. R
Director
State Institute of Health and Family Welfare
Uttar Pradesh

The primary goal of Continuing Medical Education (CME) is to ensure that Medical Officers engage in continuous learning and progression, ultimately leading to the delivery of optimal medical care for their patients. CME aims to assist Medical Officers in improving their performance in terms of patient care and satisfaction.

In the realm of healthcare, there has been a notable effort to underscore the importance of effectively managing High Risk Pregnancy and Critical Care Obstetrics among Medical Officers in Provincial Health & Medical Services. It has been observed that a lack of systematic management has led to numerous unfortunate outcomes. Therefore, there is a need for a customized CME program tailored to equip Medical Officers in Uttar Pradesh with exposure to the latest advancements in the treatment of High Risk Pregnancy and Critical Care Obstetrics.

To achieve this objective and enhance knowledge, the faculty and research team at the State Institute of Health and Family Welfare (SIHFW), Uttar Pradesh, in collaboration with the assistance of Professor Rekha Sachan and her team, King George's Medical University (KGMU) in LUCKNOW, has contributed to the development of this CME module. It is expected that this module will be widely distributed, and feedback on its effectiveness will be gathered in the coming months.

(Dr. Rajaganapathy. R)


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SECTION A


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CHAPTER-1

HYPERTENSIVE DISORDERS OF PREGNANCY

Author : Prof. Rekha Sachan

INTRODUCTION

Hypertensive disorders most common complication of pregnancy and complicate 7-15% of all pregnancies.

Preeclampsia complicates - 2-8% of all pregnancies. [1] Eclampsia complicates 0.05 – 0.5% pregnancies (1–2% of preeclampsia cases convert in eclampsia)

Fetal Complication of Pre-eclampsia: Pre-eclampsia strongly associated with fetal growth restriction(FGR), low birth weight, spontaneous or iatrogenic preterm delivery, respiratory distress syndrome (RDS), admission to neonatal intensive care and cerebral palsy.

Classification:

Hypertensive disorders of pregnancy are leading cause of maternal mortality and classified into 4 groups:

- Gestational hypertension
- Preeclampsia & eclampsia,
- Chronic hypertension and
- Pre-eclampsia superimposed on chronic hypertension.

Definition

	ACOG (2020)	NICE (2019)
Chronic Hypertension	SBP ≥ 140 or DBP ≥ 90 mm Hg <20 weeks two increased readings at least 4 hours apart or diagnosed preconceptionally or BP remains elevation >12 weeks postpartum	Hypertension that is present at the booking visit, or before 20 weeks of gestation.
Gestational Hypertension	SBP ≥ 140 or DBP ≥ 90 mmHg On 2 occasions at least 4 hours apart after 20 weeks gestation In a previously normotensive woman Absence of proteinuria or systemic signs/symptoms BP return to normal in postpartum period	New hypertension presenting after 20 weeks of pregnancy, in labor, first 24hr postpartum without significant proteinuria Resolves 3 months postpartum
Preeclampsia	**Blood pressure:** SBP ≥ 140 or DBP ≥ 90 mm Hg on 2 occasion at least 4 hours apart after 20 weeks in a women previously normal BP. SBP ≥ 160 or DBP ≥ 110(severe HTN can be confirmed within minutes to facilitates anti HTN therapy) • **Proteinuria** 300 mg or more per 24 hour urine collection or Protein/creatinine ratio of 0.3 mg/dL or more or	New onset HTN (SBP ≥ 140 or DBP ≥ 90) mmHg after 20 week and + >1 of the following: • **Proteinuria:** urine protein: creatinine ≥ 30mg/mmol or ACR ratio ≥ 8mg/mmol or atleast 1g/L (2+) on dipstick tesing • **Renal insufficiency:** S.creat ≥ 90 umol/litre or ≥ 1.02mg/100ml

	Dipstick reading of 2+ (used only if other quantitative methods not available) **• Or in the absence of proteinuria, new onset HTN with new onset of any of the following:** **Thrombocytopenia**< 1 lac platelet Count **Renal insufficiency:** Creatinine conc. > 1.1mg/dl or a doubling of Creatinine conc. In absence of other renal disease **Impaired liver function:** Elevated blood concentration of liver transaminases to twice normal **Pulmonary edema** New onset **headache** unresponsive to medication and not accounted for by alternative diagnoses or **visual** symptoms.	• ALT/AST > than 40 IU/L, Right Upper Quadrant pain • Neurological complications • Hematological complications: PLT<150000/uL

ACOG 2019

Severe range Hypertension in pregnancy	SBP≥ 160 mmHg DBP≥110 mmHg 2 readings at least 4 hours apart
Chronic Hypertension **Superimposed Preeclampsia**	Preeclampsia in a woman with a history of Hypertension before pregnancy or before 20 weeks of gestation.

Sub-Classification of Preeclampsia as per Federation of Obstetrics & Gynecology (FIGO)

Early onset PE-(with delivery at <34+0 week of gestation)

Pre term PE- (with delivery at <37+0 week of gestation)

Late onset PE- (with delivery at ≥ 34+0 week of gestation)

Term PE- (with delivery at ≥ 37+0 week of gestation)

Clinical Risk Factors Responsible for Development of Pre- eclampsia

Moderate Risk Factors-

- Nulliparity
- Obesity (body mass index greater than 30)
- Family history of preeclampsia (mother or sister)
- Sociodemographic characteristics (African American race, low socioeconomic status)
- Age 35 years or older
- Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)

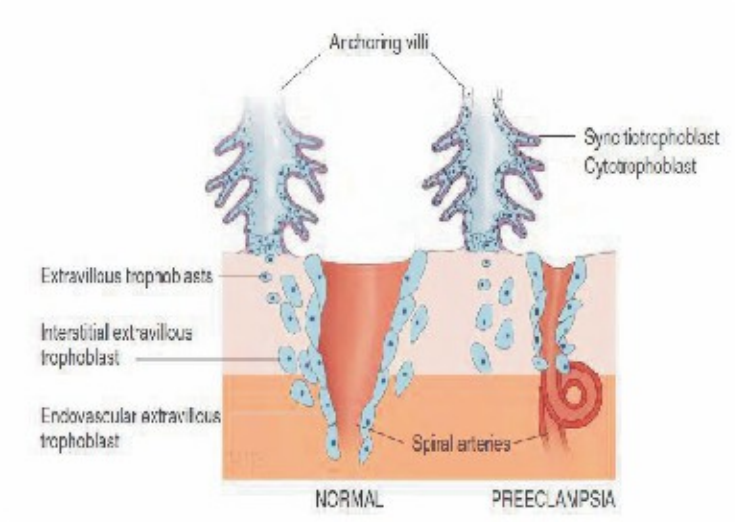
High Risk Factors

- History of preeclampsia, especially when accompanied by an adverse outcome
- Multifetal gestation
- Chronic hypertension
- Type 1 or 2 diabetes

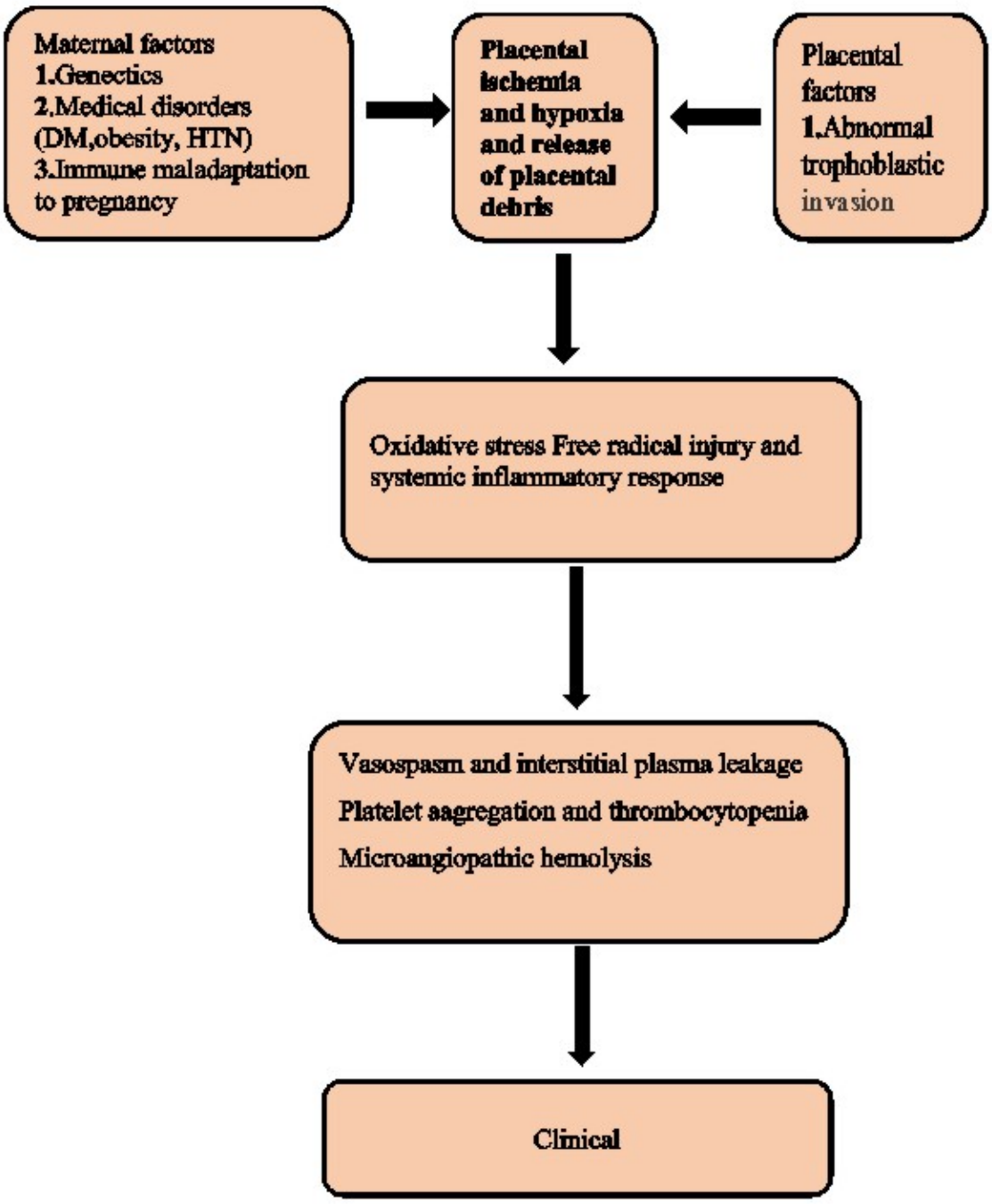
- ❖ **Renal disease**
- ❖ **Autoimmune disease (ie, systemic lupus erythematosus, the antiphospholipid syndrome)**

Etiological Factors Responsible for Development of Preeclampsia

- **Abnormal trophoblastic invasion of uterine vessels**
- **Immunological maladaptive tolerance dysfunction**
- **Maternal maladaptation to cardiovascular or**
- **inflammatory changes of normal pregnancy**
- **Genetic: Inherited predisposing genes as well as epigenetic influences (HLA DR)**



Extra villous trophoblast invades and replace the endothelial and muscular lining of spiral arterioles to form a dilated low resistance vessel. In preeclampsia there is defective implantation which leads to incomplete invasion thereby high resistance to flow.


Maternal factors
1.Genectics
2.Medical disorders (DM,obesity, HTN)
3.Immune maladaptation to pregnancy
Placental ischemia and hypoxia and release of placental debris
Placental factors
1.Abnormal trophoblastic invasion
Oxidative stress Free radical injury and systemic inflammatory response
Vasospasm and interstitial plasma leakage
Platelet aagregation and thrombocytopenia
Microangiopathic hemolysis
Clinical

Pathophysiology of Preeclampsia

- Normal pregnancy is characterized by increase plasma volume, increase cardiac output and decrease peripheral resistance.
- Usually during second trimester mean BP decreases but in hypertensive disorders of pregnancy there is change in hemodynamic of pregnancy.

Cardiovascular System

- Hypertension- greater cardiac overload
- Decrease preload
- Endothelial activation- causing interendothelial extravasation of intravascular fluid into extracellular space

Hemodynamic Changes

- Ventricular remodeling
- Diastolic dysfunction 40 -45 %
- Increase pulmonary capillary wedge pressure and pulmonary edema
- Hemoconcentration
- Thrombocytopenia
- Hemolysis – microangiopathic hemolysis
- Derranged coagulation

Kidney and Electrolytes

- Reduced renal blood flow and GFR
- Glomerular capillary endotheliosis
- Elevated plasma uric acid
- Reduced plasma oncotic pressure
- Elevated urinary sodium
- Proteinuria nonselective

- Irreversible renal cortical injury is rare
- Acute tubular necrosis-

  comorbid haemorrhage, hypovolemia and hypotension (placental abruption)

Endocrine and Hormonal Alterations

- ↑ AngiotensinII, renin and ANP

Liver Complication

Liver pain – moderate to severe

- Sign of severe disease
- Right upper quadrant/mid epigastric
- Periportal Hemorrhage
- Shock liver

Increase AST/ALT.

- Sometimes Hepatic hematoma
- Subcapsular and Capsular rupture

Prophylactic Measures for Reducing the Risk of Hypertensive Disorders of Pregnancy

1. Early identification of sign and symptoms of preeclampsia
2. **Aspirin :** Start between 11 weeks to 14 weeks 6 day, 150mg HS till 36 weeks or till delivery. (as per FIGO 2019 guideline)
3. Start aspirin 81mg/day btw 12 to 28 week (optimally before 16 weeks) till delivery if high or >1 moderate risk factor (as per ACOG 2020 guideline)
4. Aspirin (75-150mg/day) daily from 12weeks till delivery. (as per NICE2019 guideline)

5. Role of calcium supplementation: low Ca intake(<800mg/day) then give 1.5-2.0 g elemental Ca/day
6. Early identification of proteinuria
7. Offer PLGF based test between 20week to 35week.

✓ No role of using – magnesium, folic acid, antioxidants (vit C, E), fish oil, garlic.

✓ No role of low salt diet

✓ No role of bed rest

✓ Role of metformin, statins remains investigational

Feto-maternal Surveillance –Antenatal Visits

1. **In cases having Chronic hypertension**
   - Weekly if HTN is poorly controlled
   - 2 to 4 weekly if well controlled
   - Evaluate end organ involvement
   - Evaluation of maternal co morbidities- obesity, DM
2. **In patients with Pre-eclampsia/Gestational Hypertension**

Full clinical examination at each visit

Criteria for admission

1. SBP≥160mm Hg
2. any maternal biochemical, hematological derangement –

rise in creatinine (90 micromole/l *, 1mg/100ml*, 1.1mg/dl, doubling of baseline).

Alanine transaminase (70iu/l, twice of upper limit *). Fall in platelet (<1 lac/micro lt)

3. If Signs of impending eclampsia

4. If Signs of severe pre-eclampsia

5. If Fetal compromise

Antihypertensive Drugs

When to start

Guideline	DBP	SBP
ACOG[3]	>110	>160
NICE[4]	≥90	≥140

Initial regime –

T. labetolol 200mg orally every 12 hrly. Increase to 800 mg P/O every 8 to 12 hrly (max2400mg/day).

- ✓ If no control, then add oral short acting nifedipine and increase the dose gradually. Goal: maintain BP at 130-150 / 90-100 mm Hg)
- ✓ (To reduce end organ damage & prevent morbidity
- ✓ Loop Diuretics should be avoided (used antepartum only to treat pulmonary oedema)
- ✓ ACE inhibitors, diuretics C/I in pregnancy
- ✓ No significant difference regarding efficiency or safety between labetalol and hydralazine or between hydralazine and calcium channel blocker (CCB)
- ✓ Oral Labetalol and CCB have been commonly used

Commonly used antihypertensive for urgent control of BP

Drug	Dosage	MOA	Adverse effects
Hydralazine	10 mg initial dose f/b 10 mg every 15 mins	Centrally acting	Dry mouth, somnolence, pos tural hypotension
Labetalol	20 mg iv bolus f/b 40 mg the n 80 mg every 10 min Max: 220mg	Combined α and β blocker, not ass ociated with IUG R	Discontinue if signs of liver dysfunction, asthma, CHF
Nifedipine	10mg immediate f/d 10-20 mg within 20 to 30 min	Dihydropyridine calcium channel blocker-vasodilatation by smooth muscle r elaxation	Headache, edema, allergic h epatitis, usage with MgSo4 n euromuscular blockade
Atenolol	50-100 mg PO od	β1 blocker	IUGR, mask symptoms of acute hypoglycemia

INTRAPARTUM MONITORING

Seizure prophylaxis

In pre-eclampsia and gestational HTN with severe features and in patients with Eclampsia

- ✓ Drug of Choice -MgSO4 in intrapartum and postpartum period.
- ✓ Acute BP shoot up has to be controlled by parenteral medication

- ✓ BP during labor should be monitored hourly with controlled hypertension
- ✓ In cases with uncontrolled BP it should be monitored-At interval of - 15 -30 min until BP<160/110mmHg
- ✓ Continue antihypertensive medication during labor
- ✓ Very close monitoring of biochemical parameters in severe cases - 12 hourly lab testing in HELLP
- ✓ MgSo4 coverage to be continued during labor / surgery and 24 hr postpartum

Termination

	Preeclampsia/ Gestational HTN/Chronic HTN without severe features	With severe feature
POG	Till 37+ 0/7 weeks	34 +0/7 wk after maternal stabilization or with labor, PROM. Should not be delayed due to steroid coverage

Magnesium Sulphate

Route of administration: IM, IV

Uses – anticonvulsant

- neuroprotection

Monitoring during therapy

- Deep tendon reflex (knee jerk)
- Respiratory rate (>14/min)
- Urine output (>30ml/hr)
- Falling oxygen saturation indicates respiratory depression

Post-Partum

Monitoring Immediate

- ✓ Continue BP monitoring
- ✓ Continue anti-hypertensive
- ✓ Continue mgso4 for 24 hr postpartum

Eclampsia

- ✓ Convulsive manifestation of hypertension
- ✓ New onset tonic –

clonic, focal , multifocal seizure , in absence of other causative condition

Parameters Monitored During Foetomaternal Survillance

	Gestational HTN Non severe pre-eclampsia Controlled chronic HTN	**Severe preeclampsia Chronic HTN with superimposed pre eclampsia**
Clinical	weight gain , headache ,visual symptoms, epigastric pain	weight gain, headache , visual symptoms , epigastric pain
BP	Daily 4 hrly except between 12 AM to 6 AM, unless previous readings are elevate. Once/twiceweekly well cont Chronic HTN, every 48hr or more in NSPE (targe t≤135/85)	15min-30min when acute 4hrly thereafter. Target ≤135/85 mm Hg
Proteinuria	On admission. Every 2 days thereafter (new- no role after diagnoses in preeclampsia) For Gestational HTN- once/twice /week -once /week (ACOG)	Severe gestational HTN-daily

Blood test	Weekly Twice / week	Sooner depending on disease progression. 3 times /week 12hrly in HELLP
AFI	2-4 week	2 weeks
CTG	Only if indicated	At diagnosis and when indicated Repeat –if changes observed in fetal movement , vaginal bleeding , abdominal pain , deteriorating maternal condition
Umbilical artery doppler	28wk, 32 weeks, 36weeks gestation in chronic hypertension 2to 4 weekly in Gestational HTN, NSPE	2 weeks

Management	
Immediate care	Maintain airway Left lateral position Oxygen & ventilator (if needed, 8-10l/min) Fluid therapy to maintain circulation
	Summary
Specific management	MgSo4 Anticonvulsant Antihypertensive drugs Diuretics (pulmonary edema)
Delivery	Treatment of choice **Caesarean** – prolong fetal bradycardia poor bishop Gestation < 30 week FGR Poor BP control

Regimen of MgSO4

	Zuspan	Pritchard
Dosing	Loading dose 4g IV over 15-20 min 1 g/hr. IV infusion (maintenance)	Loading dose 4g (20% solution) IV over 5 min and 5g IM (50% sol) into each buttock 5g of 50 % solution IM every 4 hr into alternate but tock, deeply, outer upper quadrant Addition of 1ml of 2% lidocaine minimizes discomfort.

HELLP

- ✓ A complication of severe preeclampsia and eclampsia
- ✓ It is characterized by (haemolysis, elevated liver enzymes and low platelet counts)
- ✓ Hemolysis (at least two of these)
- ✓ Abnormal peripheral smear (schistocytes, burr cell, echinocytes, etc)
- ✓ Increased total bilirubin (mostly indirect form) >1.2 mg/dl
- ✓ Low serum haptoglobin level
- ✓ Drop in hemoglobin level unrelated to blood loss
- ✓ Increased lactate dehydrogenase >600IU/L
- ✓ Elevated liver enzymes
- ✓ Increased transaminases (AST and ALT) >70 IU/L (twice the upper limit of normal)
- ✓ Thrombocytopenia
- ✓ Platelet count <100,000-150,000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CHAPTER-2

GESTATIONAL DIABETES MELLITUS

Author : Prof. Rekha Sachan

Introduction

Diabetes Mellitus is a disorder of carbohydrate metabolism. It is caused by a combination of hereditary and environmental factors, and is characterized by either inadequate secretion or inadequate action of insulin.

Definition-

➔ Gestational diabetes mellitus has been defined as impaired Glucose Tolerance with onset or first recognition during pregnancy. (**ACOG-American collegeof** Obstetrics & Gynecology 2013)

➔ GDM is diabetes that is first diagnosed in second or third trimester of pregnancy that is not clearly pre-existing type 1 or type 2 diabetes. (**American** diabetic association **(ADA)** update 2020)

Incidence - 1 in 10 pregnancies are associated with diabetes and out of these 90% are GDM

Prevalence - As per Ministry of Health & Family Welfare (MOHFW), Government of India (GOI) 2018 data Gestational diabetes mellitus prevalence is 10-14.3%.

Women with GDM and their offspring are at increased risk of developing type II Diabetes Mellitus later in life.

Maternal complications of GDM

- Polyhydramnios
- Pre-eclampsia

- Prolonged labor
- Obstructed labor
- Uterine atony
- Postpartum hemorrhage
- Puerperal infection

Fetal complications of GDM

- Spontaneous abortion
- Congenital malformation
- Intra-uterine death
- Stillbirth
- Shoulder dystocia
- Birth injuries
- Neonatal hypoglycemia
- Respiratory distress syndrome

Diagnosis of GDM

DIPSI TEST (Diabetes in pregnancy study group of India) is main diagnostic test to diagnose Gestational Diabetes mellitus

- This is single step testing using 75 g oral glucose & measuring capillary glucose 2 hour after ingestion of glucose
- 75g glucose is dissolved in 300ml water & given orally in 5 min irrespective of whether the pregnant women come in a state of fasting or non-fasting.
- Plasma standardized glucometer to be used to evaluate blood glucose

- If vomiting occurs within 30 min of oral glucose intake, test has to be repeated the next day
- If vomiting occurs after 30 minutes, the test continues
- Plasma glucose level ≥140 mg/dL is taken as cut off for diagnosis of GDM

Management of GDM- Management of GDM

Management of GDM includes medical nutrition therapy, oral hypoglycemic agent, and Insulin either Mixtard or regular humane insulin

Medical Nutrition Therapy (MNT) & Exercise for GDM

- Medical Nutrition Therapy (MNT) & exercise forms the mainstay for treatment of GDM
- All who test positive for GDM should be started on MNT and exercise for 2 weeks
- After 2 weeks a 2-hour Postprandial glucose (PPG) (post lunch) should be done
- If 2 hour PPG ≤120mg/dL repeat test every 2 weeks in second trimester & every week in third trimester
- If 2 hour PPG ≥120mg/dL medical management should be started along with MNT

Medical Management of GDM

- Metformin or Insulin therapy is the accepted Medical management for GDM if not controlled on MNT
- At PHC, Medical Officer should initiate treatment

- Pregnant women with GDM should be referred to District Hospitals/ Medical Colleges if:
  - blood sugar levels are not controlled on 20 U Insulin/ Day or 2 g Metformin/day
  - there is some other complication
- At CHC/ District Hospitals/Medical Colleges a specialist/ Gynecologist / Physician/MO can start metformin or insulin

Role of Metformin in Management of GDM

- Metformin can be started only after 20 weeks
- Dose - started with 500 mg twice daily, maximum dose 2 gm/ day
- If blood sugar is not controlled with the maximum dose of metformin & MNT + exercise, Insulin is to be added

Side effects

- GI symptoms eg. Diarrhea, nausea, stomach pain, heartburn
- Lactic acidosis
- Low blood sugar

Role of Insulin in Management of GDM

- Insulin can be started any time during pregnancy
- Insulin mixtard (30:70) is preferred & dose is titrated according to blood sugar levels

Blood sugar levels	Dose of Insulin
120-160 mg%	4 U
160-200 mg%	6 U
>200 mg%	8 U

- Repeat fasting blood sugar(FBS) & 2-hour postprandial blood sugar(PPBS) every 3rd day or more frequently till dose of insulin adjusted
- If Insulin is required in high doses, metformin may be added to the treatment
- Pregnant women on Insulin should be instructed to keep sugar/jaggery/glucose powder handy to treat hypoglycemia

When to Pregnant women with GDM refer to a higher center?

- If persistent Nausea & vomiting and patient is not able to take food orally
- Fasting blood glucose >200mg/dL with or without insulin
- Fasting blood glucose >150 mg/dL or post breakfast > 250 mg/dL even after giving insulin is uniformly required.
- Total dose of insulin (combined morning and evening dose) on each day exceeds 20 units
- If pregnant women develop low blood glucose (hypoglycemia) more than once in a day
- If pregnant woman refuses to take insulin injection at home

Requirement of Obstetric care for pregnant women with GDM-

- Antenatal care should be provided by gynecologist/ EmOC trained doctor if available
- GDM diagnosed before 20 weeks: Fetal anatomical survey mandatory at 18-20 weeks

- All GDM- Fetal growth scan should be done at 28-30 weeks & 34-36 weeks
- pregnant women with GDM having well controlled blood glucose level & without complications should receive Routine antenatal care as per GOI guidelines
- pregnant women with GDM having uncontrolled blood glucose level or any other complication, Frequency of ANC visits should be increased to every 2 weeks in second trimester & every week in third trimester
- Monitor for abnormal fetal growth (macrosomia/growth restriction) and polyhydramnios at each ANC visit & auscultate Fetal heart
- Counsel pregnant women about the importance of Daily fetal movement counts (DFMC)
- Monitoring of mother should be done & to check for development of hypertension in pregnancy, proteinuria and other obstetric complications.

Role of Antenatal steroids for Fetal lung maturity

- Steroid coverage should be given in pregnant women with GDM between 24-37 weeks of gestation and requiring early delivery
- Inj. Dexamethasone 6 mg IM 12 hourly for 2 days (total 4 doses)
- Ideally pregnant women to be admitted in hospital
- More vigilant monitoring of blood glucose levels required for 5-7 days & during steroid coverage
- In case of raised blood glucose levels during this period, adjustment of insulin dose should be made accordingly

Place of Delivery of GDM women

- pregnant women with GDM with good control of Blood glucose (2 hr PPBG< 120 mg/dl) levels may be delivered at their respective health facility

- pregnant women with GDM on insulin therapy with uncontrolled blood glucose levels (2 hour PPG ≥120 mg/dl) **or**

insulin requirement >20 U/day should be referred for delivery at CEmONC centres under care of gynecologist at least a week before the planned delivery.

Time of Delivery in Women Suffering from GDM

- pregnant women with GDM with well controlled plasma glucose:
- If not delivered spontaneously, induction of labour should be done at or after 39 weeks' pregnancy pregnant women with GDM with poor plasma glucose control, those with risk factors like hypertensive disorder of pregnancy, previous still birth & other complications, deliver earlier and Timing of delivery should be individualized by the obstetrician.

Mode of Delivery in women suffering from GDM

Vaginal delivery should be preferred and LSCS should be done for obstetric indications only in case of fetal macrosomia (estimated fetal weight > 4 Kg) consideration should be given for a primary cesarean section at 39 weeks to avoid shoulder dystocia.

What Special precautions should be taken during Labor

- pregnant women with GDM on Metformin or Insulin require blood sugar monitoring during labor by a glucometer
- Morning dose of insulin/metformin is withheld on the day of induction/labor and 2 hourly blood sugar monitoring should be done
- Normal Saline infusion should be started & regular insulin should be added according to requirement /blood sugar levels

Neonatal care of babies of GDM Mother

- All neonates should receive essential newborn care
- Emphasis on early breastfeeding to prevent hypoglycemia
- Monitor newborns for hypoglycemia
- Start monitoring 1 hr after delivery & continue every 4 hours (prior to next feed) till four stable glucose values are obtained
- Cut off of capillary blood glucose for hyoglycemia in normal birth weight newborn is <45 mg/ dL and in IUGR <54 mg/dL
- Evaluate neonate for other neonatal complications like respiratory distress, convulsions, hyperbilirubinemia

Requirement of Post-delivery follow up in GDM

- Women with GDM should be offered regular postpartum care after delivery
- 75 g Oral glucose tolerance test (OGTT) should be performed after 6 weeks
- Woman with normal OGTT is counselled about lifestyle modifications, weight monitoring & exercise. Advise women to get annual screening for Diabetes Mellitus in NCD clinic as per protocol.
- Test positive Woman should be linked with NCD program for further management.
- Pregnant women with GDM and their offspring are at increased risk of developing Type II Diabetes mellitus in later life. They should be counselled for healthy lifestyle and behavior, particularly role of diet & exercise.

CHAPTER-3

ANEMIA IN PREGNANCY

Author : Dr. Shilpa Singh

Definition

Anemia is qualitative or quantitative reduction in the oxygen carrying capacity of blood usually resulting from reduced hemoglobin that leads to reduced oxygen supply to peripheral tissues. World health organization (WHO) has defined anemia in pregnant women as hemoglobin (Hb) concentration of less than 11g% and hematocrit (HCT) of less than 33% at any time during pregnancy and in postpartum period as Hb < 10 g%. The Center for Disease Control and Prevention (CDC) proposes a cutoff Hb value of 11g% in 1st and 3rd trimesters and 10.5g% during 2nd trimester.

Magnitude of Problem

Anemia is the most common medical disorder during pregnancy, resulting in increased maternal morbidity and mortality. According to National Family Health Survey-4 (2015-2016), prevalence of anemia in pregnancy is 50.3%.

According to WHO, 32.4 million pregnant women suffer from anemia worldwide out of which 50% cases are attributable to iron deficiency anemia (IDA).

Globally 5,91,000 perinatal deaths and 1,15,000 maternal deaths occurred due to IDA.

Severity of Anemia in Pregnancy

According to WHO and Indian Council of Medical Research (ICMR), severity of anemia is graded as: mild, moderate and severe, Table 1[2]

Table 1: Severity of Anemia in Pregnancy

	WHO	ICMR
Mild	10-10.9	10-10.9
Moderate	7-9.9	7-10
Severe	<7	7-4
Very Severe		<4

Etiology

- Physiological Anemia: It serves to reduce the blood viscosity which enhances placental perfusion and facilitates transfer of nutrients and oxygen delivery to fetus. It has following characteristics Hb >10g%,
- HCV>30%, RBC count>3.2 million with normal RBCs morphologically.

Acquired:

- Nutritional: Iron deficiency, folate and vitamin B12 deficiency.
- Anemia of chronic disease: For example, chronic malaria, TB, chronic renal disease.
- Bone marrow insufficiency: Due to drugs, radiation. Chronic blood loss from any site, e.g. bleeding piles, hookworm infestation
- Hereditary: Thalassemia, sickle cell anemia, hemoglobinopathies, hereditary hemolytic anemia

Management and Approach to Anemia (Table 2)

- ✓ Confirm the diagnosis Grade the severity
- ✓ Find out the type of anemia
- ✓ Investigate for the cause of anemia and treat the cause
- ✓ Build up the iron stores.

Iron Deficiency Anemia (IDA)

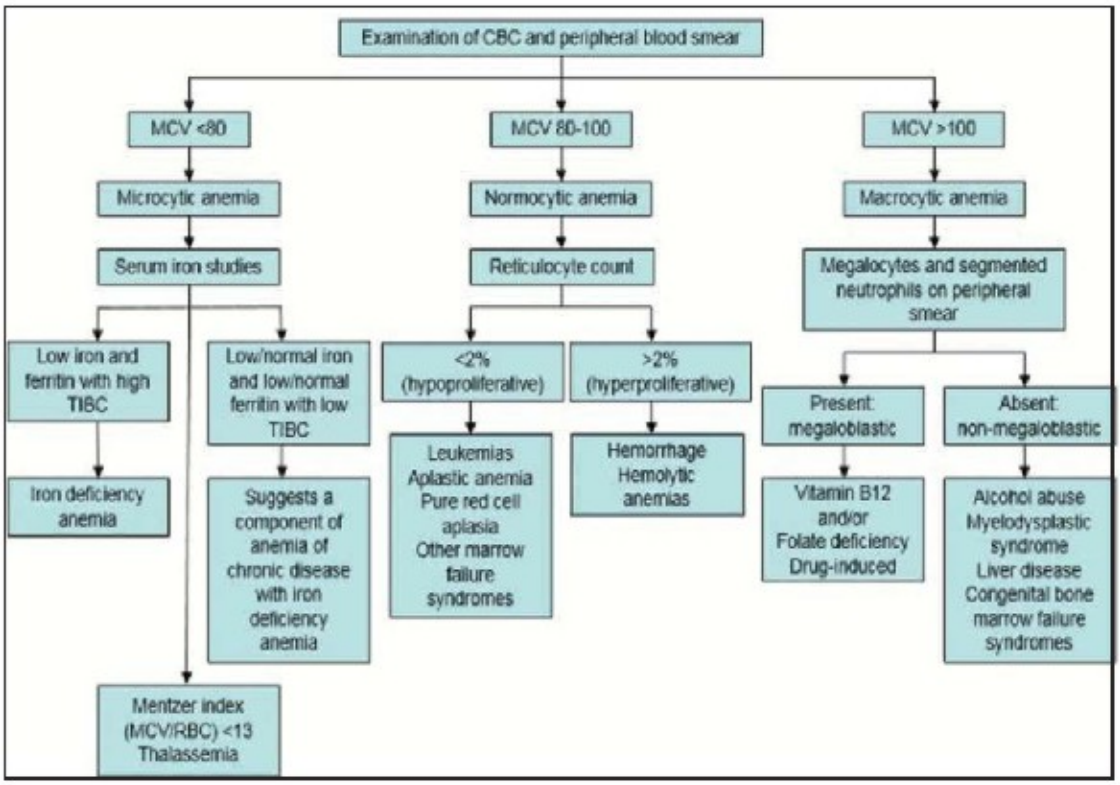
IDA is the most common type of anemia in pregnancy. The nutritional status of women depends on long term iron balance and is favored by ingestion of adequate amounts of iron in the diet and through iron supplementation.

Average iron requirement is 4mg/day throughout pregnancy varying from 0.8 mg/day in 1st, 4 mg/day in 2nd and 6 mg/day in 3rd trimester.

Iron stores depletion is the earliest stage in which storage iron is decreased or absent but serum iron concentration, transferrin saturation and blood hemoglobin levels are normal.

Iron-deficient erythropoiesis is characterized by decreased or absent storage iron, usually low serum iron concentration and transferrin saturation, but without frank anemia.

Table 2: Approach to Anemia



Iron deficiency anemia is the most advanced stage of iron deficiency and is characterized by decreased or absent iron stores, low serum iron concentration, low transferrin saturation and low blood hemoglobin concentration.

Causes of Iron Deficiency Anemia in Pregnancy

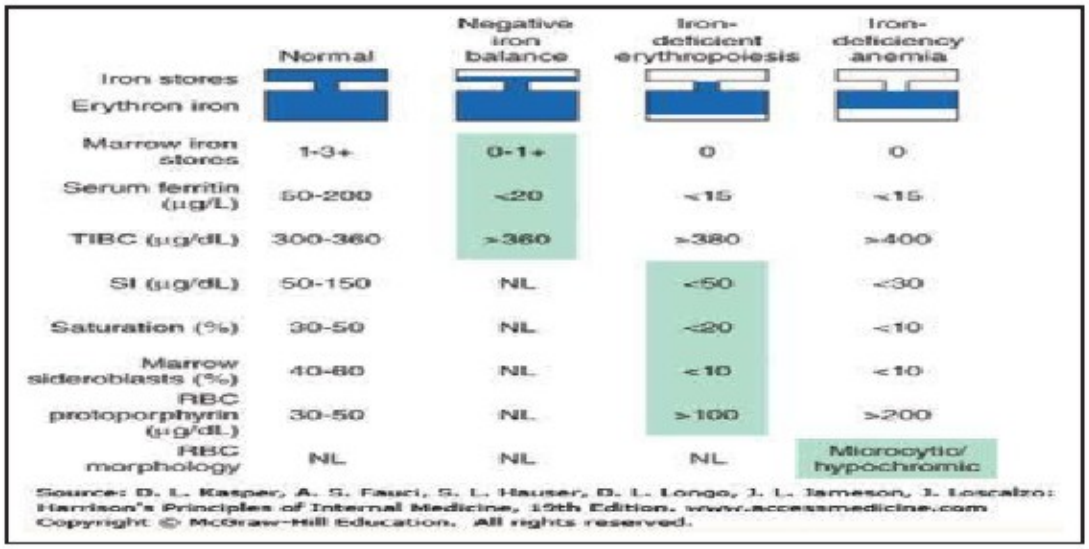
Increased demand: Net increase in iron expenditure is approximately 900mg.

Dietary deficiency: Most common cause of IDA in India.

Impaired absorption

Increasedblood loss: Hookworm infestation, Multiple pregnancies.

Table 3: Stages of Iron Deficiency Anemia



Source: D. L. Kasper, A. S. Fauci, S. L. Hauser, D. L. Longo, J. L. Jameson, J. Loscalzo: Harrison's Principles of Internal Medicine, 19th Edition. www.accessmedicine.com

Diagnosis

- Complete blood count includes Hb, RBCs indices, reticulocyte counts, platelet count and TLC Peripheral blood smear
- Urine microscopy and culture Stool for occult blood and ova cyst

Table 4: Effect of Anemia on Pregnancy

Antepartum complications	Intrapartum complications	Postpartum complications	Fetal outcome
Increased risk of preterm delivery Premature rupture of membranes	Prolonged labor Increased rates of operative delivery and induced labor Fetal distress	Postpartum hemorrhage Puerperal sepsis Lactation failure Pulmonary	Low birth weight Prematurity Infections Congenital
Preeclampsia	Abruption	Thromboembolism	malformation Neonatal anemia
Intrauterine Death Antepartum hemorrhage	Inability to stand even slight blood loss	Subinvolution of uterus Postpartum depression	Abnormal cognitive development
Congestive heart failure	Anaesthesia risk		Increased risk of Schizophrenia

Table 5: Clinical Features of Iron Deficiency Anemia

General Symptoms Mild anemia: usually asymptomatic Moderate anemia: weakness, fatigue, lassitude, exhaustion, loss of appetite, indigestion, giddiness, breathlessness Severe anemia: palpitations, tachycardia, breathlessness, generalised edema	**Specific Symptoms** Ingestion of non-nutritive materials such as clay, dirt, paper, laundry starch (pica) Lead paint by children, pagophagia (ice craving) Hair loss and restless legs syndrome
General Signs No signs in mild anemia Pallor, nail changes (depressed nails, koilonychia), cheilosis, glossitis, stomatitis, edema, hyperdynamic circulation as evidenced by short and soft systolic murmur, signs of congestive heart failure (decompensated anemia), fine crepitations at bases of lungs due to congestion	**Specific Signs** Pallor, decreased papillation of the tongue, cheilosis, and Brittle, fragile and longitudinally ridged nails koilonychia, Platynychia

NESTROFT (naked eye single tube red cell osmotic fragility test) & LFTs

- Iron studies
- Investigations to rule out other causes of anemia
- The management starts from childhood.

- Dietary modification: consumption of iron rich food, cooking food in iron utensils and avoidance of excessive tea, coffee and overcooking of food
- Food fortification with iron (wheat flour, salt): Of various fortifying iron compounds, sodium iron ethylenediaminetetraacetic acid (NaFeEDTA) is most frequently used owing to its effectiveness with a diet rich in phytate such as sugar, curry powder, soy sauce, fish sauce and maize flour. Micronized ground ferric pyrophosphate is another iron salt used for fortification of color-sensitive food vehicles, such as salt in Africa and rice in India.
  - Screening of adolescent girls and iron Supplementation wherever required
  - Hookworm and malaria

Chemoprophylaxis Adequate birth spacing (minimum of two years)

Table 6: Summary of recommendations by WHO and MoHFW

	During Pregnancy		Postpartum
	Prophylaxis	Treatment	
WHO	Daily 60 mg iron + 400 µg folic acid till term	Daily 120 mg iron + 400 µg folic acid till term	Daily 60 mg iron and 400 µg folic acid - 3 months
MoHFW	Daily 100 mg iron + 500 µg folic acid - for 100 days starting after the first trimester, at 14-16 weeks of gestation	• Mild anemia - 2 IFA tablets/day - 100 days • Moderate anemia – IM iron therapy + oral folic acid	Daily 100 mg iron + 500 µg folic acid - 6 months

Anemia Management Protocol for Pregnant Women

- ✓ All pregnant women to be screened at each ANC visits
- ✓ If Hb: 10–10.9 g/dl (mild anemia) or Hb 7–9.9 g/dl (moderate anemia):

2 tablets IFA (100 mg elemental Iron, 500 mcg Folic Acid) daily, orally

OR

IV Iron Sucrose or Ferric Carboxy Maltose (FCM) late in pregnancy or in case of non-compliance Follow up after 2 months

- If Normal Hb – continue IFA Prophylaxis
- If Hb is not improved (< 1g/dl rise in one month) – Investigate / refer

✓ If Hb: 5.0–6.9 g/dl (severe anemia) –
Hospitalization, Evaluation, Blood transfusion

Treatment

The aim of treatment is to raise the Hb levels to near normal followed by restoration of iron stores before she goes into labor. The route of administration of iron depends upon the severity of anemia, duration of pregnancy and any other factors.

Oral Iron Therapy

180-200 mg elemental iron is given daily in divided doses. Iron is absorbed best empty stomach but causes lot of gastric irritation. Alternatively, it can be advised to take before meals or after 1 hour of meals. Vitamin C enhances the absorption of oral iron and tea, coffee, milk and calcium supplements can decrease iron absorption. Compliance is checked by asking the color of stools, which should be black.

A repeat Hb is advised after 3-4 weeks of oral therapy and once Hb reaches normal levels, prophylactic daily iron supplementation is recommended for at least 6 months during pregnancy and should be continued in postpartum period for 6 more months.

Response to Iron Therapy (Table 7)

Patients adequately responding to oral iron will show some clinical improvement with a sense of improved well-being, lesser palpitations and fatigue, increased effort tolerance, better sleep etc. Optimal response Hb > 2g% increase in 3 weeks

Table 7: Response to Iron Therapy

5-7 days	Reticulocyte count increases (0.2% per day)
2-3 weeks	Hb increases by 0.8-1g% per week RBC indices improve
6-8 weeks	Hb comes to normal range RBCs become normocytic, normochromic on smear S. Ferritin increases

Elemental Iron in Oral Iron Preparations

Percentage of elemental iron is highest in Carbonyl iron preparations followed by Ferrous Fumarate and Ferrous Sulphate, Table 8. Ferrous salts are preferred because they are absorbed (thrice) much more readily.

Ferrous Sulphate is used commonly because it is least expensive and has high elemental iron. Ferrous Fumarate is better tolerated.

Table 8: Elemental Iron in Various Oral Iron Preparations

Various Oral Iron Preparations			
Preparation	**Total Iron (mg/tab)**	**Elemental Iron (mg/ tab)**	**% Elemental Iron**
Ferrous Fumarate	200	66	33
Ferrous Sulphate Hydrous	300	60	20
Ferrous Sulphate Desiccated	200	65	32
Ferrous Succinate	100	35	35
Ferrous Ammonium Citrate	160	30	18
Ferrous Ascorbate	730	100	14

Parenteral Iron Therapy (Table 9 &10)

The rise in Hb after parenteral therapy is 0.7-1.0g% per week which is same as seen with oral iron therapy. The main advantage of parenteral therapy is the certainty of its administration and bioavailability. The indications of parenteral iron are:

- Intolerance to oral iron
- Impaired iron absorption
- Chronic blood loss
- Gastrointestinal disorders which gets aggravated by oral iron-peptic ulcer disease, ulcerative colitis
- After 32 weeks period of gestation, parenteral iron is preferred as the compliance is 100%
- With erythropoietin for faster absorption.

The contraindications of parenteral iron are:

- History of anaphylactic reactions
- First trimester of pregnancy
- Chronic liver disease
- Active infection.

Oral iron should be stopped 24 hours prior to starting parenteral iron to avoid toxic reactions.

Table 9: Various Parenteral Iron Preparations

Preparation	FDA Category	Strength	Route of Administration
Iron Dextran	C	2 ml/amp 50 mg/ml	IM/IV
Iron Sorbitol	B	1.5 ml/amp 50 mg/ml	IM
Iron Sucrose	B	5 ml/amp 20 mg/ml	IV
Iron Carboxymaltose	C	2 ml and 5 ml vials 50 mg/ml	IV

Formulas for Parenteral Iron Dose Calculation

Ganzoni Formula[4]

Required iron dose in mg = 2.4 x (Target Hb – Patient's Hb) x weight in kg + 1000 (for replenishment of stores)

200 mg of iron sucrose is dissolved in 200 ml normal saline and transfused over 20 minutes intravenously. Patient receives 3 doses in a week of 200 mg each.

Management of Severe Anemia in Labor

The hemoglobin levels at the time of delivery should be at least 7g %, Table 11. Patient requires 1 or more packed cell volume; each should be transfused slowly over 4–6 hours.

Table 10: Advantages & Disadvantages of Parenteral Iron Preparations

Generic Name	Content	Advantage	Disadvantage
Iron dextran	Colloidal solution of ferric hydrochloride complex with polymerase dextran	Can be given IM or IV, Total dose infusion possible	3-4 weeks for complete absorption Anaphylaxis (test dose required) More systemic toxicity
Iron sorbitol citrate complex	Iron sorbitol citric acid complex	Completely and rapidly absorbed	Only IM Binds transferrin and may saturate it multiple injections required for the total dose
Iron sucrose	Ferric hydrochloride saccharide complex	Minimal risk of anaphylaxis (<.002%), other side effects No test dose required Does not overload transferrin	Only IV Cannot be given as total dose infusion
Ferric carboxy-maltose	Does not contain dextran	Anaphylaxis is rare. No test dose required	Only IV Costly

Table 11: Indications of blood transfusion in pregnancy

Antepartum Period

1. Pregnancy <34 weeks
   a. Hb <5 g/dL with or without signs of cardiac failure or hypoxia
   b. Hb 5-7 g/dL - in presence of impending heart failure
2. Pregnancy >34 weeks
   a. Hb <7 g/dL even without signs of cardiac failure or hypoxia
   b. Severe anemia with decompensation
3. Anemia not due to hematinic deficiency
   a. Hemoglobinopathy or bone marrow failure syndromes

b. Hematologist should always be consulted

4. Acute hemorrhage
   a. Always indicated if Hb <6 g/dL
   b. If the patient becomes hemodynamically unstable due to ongoing hemorrhage

Intrapartum Period

a. Hb <7 g/dL (in labor)
b. Decision of blood transfusion depends on medical history or symptoms

Postpartum Period

a. Anemia with signs of shock/acute hemorrhage with signs of hemodynamic instability.
b. Hb <7 g% (postpartum): Decision of blood transfusion depends on medical history or symptoms

Management of 1st Stage of labor

- Counselling and consent
- Propped up position
- Oxygen should be given if required
- Minimizing the number of vaginal examinations
- Monitor for signs of cardiac failure-pulse, BP, Intermittent chest auscultation
- Fluid restriction, blood transfusion under diuretic cover
- Antibiotic prophylaxis

Management of 2nd Stage of labor

- Prophylactic ventouse or forceps delivery to cut short the 2nd stage of labor and bearing down
- Strict asepsis to be maintained

- Oxytocin if required should be given in concentrated form to avoid fluid overload
- Restrict intravenous fluids

Management of 3rd Stage of labor

- Active management of third stage of labor
- Look for any genital trauma
- Intravenous frusemide given after delivery to decrease cardiac load

Puerperium

- Watch meticulously till 6 hours postpartum for any signs of failure
- Early ambulation is advised
- Prophylactic antibiotics can be considered
- Adequate rest
- Correction of anemia-blood transfusion or iron tablets
- Contraceptive advice


राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
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ज्ञानावृते न मुक्तिः

CHAPTER-4

HEART DISEASES IN PREGNANCY

Author : Prof. S.P. Jaiswar

Cardio-obstetrics has emerged as an important multidisciplinary field that requires a team approach to the management of cardiovascular disease (CVD) during pregnancy

Incidence - 0.1 – 4.0 %, disease

Cardiovascular disease is the leading cause of pregnancy-related mortality.

Maternal mortality due to CVD is on rise due to increasing numbers of women at advanced maternal age, with preexisting comorbid conditions such as diabetes mellitus and hypertension, undertaking pregnancy

Etiological Classification of Heart Disease

Rheumatic HD (90-95%)

-MS most common

-MR (Mitral Incompetence)

-AS, AR

Miscellaneous HD

-Mitral valve prolapse

-Cardiac Arrhythmias

-Cardiomyopathy

-Ischemic Heart Disease

-Hypertensive Heart Disease

Congenital HD

***Noncyanotic Lesions**

- ASD, VSD, PS and

-Coarctation of aorta

***Cyanotic Lesions**

-Fallot's tetralogy

-Eisenmenger's Syndrome

-Developed countries –

CHD is common

Developing countries – RHD is still more common (90- 95%),
with MS prominent lesion (90%)
Congenital heart disease with pregnancy is increasing – advancement in cardiac surgery.

Approach

For **Antenatal, Intrapartum and Postpartum management** of patients with heart disease, it is important to –

Understand the cardiovascular changes during pregnancy

Risk assessment for women with heart disease

Risk should be reassessed during pregnancy and Intrapartum period using all of the following:

Comprehensive clinical assessment, including history and physical examination

modified WHO classification of risk (mWHO) NHYA functional class

Table 1. Cardiovascular Changes in a Normal Pregnancy*

	First Trimester	Second Trimester	Third Trimester	Stage 1 Labor	Stage 2 Labor	Early Postpartum	3–6 months Postpartum
Cardiac output	↑5–10%	↑↑35–45%		↑30%	↑↑50%	↑↑↑60–80% immediately, then rapidly decreases within the first hour	Return to prepregnancy values
Heart rate	↑3–5%	↑10–15%	↑15–20%	During uterine contractions: ↑40–50%		↓5–10% within 24 hours; continues to decrease throughout the first 6 weeks	Return to prepregnancy values
Blood pressure	↓10%	↓5%	↑5%	During uterine contractions: ↑SBP 15–25% ↑DBP 10–15%		↓SBP 5–10% within 48 hours; may increase again between days 3–6 due to fluid shifts	Return to prepregnancy values
Plasma volume	↑	↑↑40–50%		↑	↑↑	↑↑↑500 mL due to autotransfusion	Return to prepregnancy values

Critical periods:

- ✓ 6-8 weeks-changes start
- ✓ 28-30 weeks -max changes occur
- ✓ Intra partum period
- ✓ Just after delivery
- ✓ Second week of puerperium

Pre-conceptional Counselling

- Discussion regarding optimum time to become pregnant
- Evaluate the risk of pregnancy by modified WHO score (mWHO)
- Establish baseline functional status of heart using NYHA grading
- Effects of cardiac condition on pregnancy and the effects of pregnancy on cardiac condition
- Optimize her cardiac status by medical or surgical means
- Discontinue teratogenic drugs like ACE Inhibitors, warfarin
- Identify any additional risk factors and their likely complications

- Explain the risk of having a child with same or different cardiac lesion in case of CHD
- WHO class 1 indicates low risk, WHO class 2 indicates an intermediate risk, WHO class 3 indicates high risk, and WHO class 4 indicates a contraindication for pregnancy
- Conditions which are contraindications to pregnancy include- PAH including Eisemenger syndrome, EF < 30%, NYHA gr III-IV, Previous peripartum cardiomyopathy with residual LV dysfunction, Severe AS Severe MS, Marfan syndrome with Aortic dilatation>45 mm, Vascular Ehlers Danlos, Severe Coarctation
- WHO Class 3 and 4 are associated with highest risk of maternal mortality (25-50%)
- Women in WHO class I & II should be assessed each trimester, and those in class III and IV assessed monthly
- WHO Class 3 and 4 should be followed and delivered at an Expert center for pregnancy and cardiac disease

CARPREG risk predictors	Score
Prior cardiac event (heart failure, transient ischaemic attack, stroke before pregnancy or arrhythmia)	1
Baseline NYHA functional class >II or cyanosis	1
Left heart obstruction (mitral valve area <2 cm^2, aortic valve area <1.5 cm^2 or peak left ventricular outflow tract gradient >30 mm Hg by echocardiography)	1
Reduced systemic ventricular systolic function (ejection fraction <40%)	1

Total score	Maternal cardiovascular risk
0	5%
1	27%
≥1	75%

Factors in pregnancy – the risk of failure

- Anemia
- Infections

- Hypertension
- Hyperthyroidism
- Multiple pregnancy (↑ cardiac output 30% more)
- Caffeine, alcohol intake
- Stress
- Drugs – tocolytic

Changes in normal pregnancy may mimic heart disease

Symptoms – breathlessness, weakness,

- oedema, syncope Increase in HR

- JVP waves are more prominent
- Displacement of apex beat – upwards and laterally
- S1 may be loud, Splitting of 1st heart sound
- Ejection Systolic murmur- may be heard in 90 %
- Mammary souffle over the breast
- ECG shows left axis deviation & mild ST changes

Diagnosis of heart disease

Symptoms:

- Progressive dyspnoea
- Orthopnoea
- PND
- Palpitation
- Haemoptysis
- Syncope
- Chest pain

Signs:

- Cyanosis
- Clubbing
- Persistent neck vein distension
- Loud diastolic murmur
- Systolic murmur grade 3/6 or greater
- Cardiomegaly
- Arrhythmia
- Persistent- split second sound

Investigations

ECG – cardiac arrhythmias, hypertrophy

Echocardiography – Gives details of

- Structural anomalies

-Valve area and thus severity of disease

- Ventricular function

X-ray chest – cardiomegaly, vascular prominence

New York Heart Association classification

Class I: No limitation of physical activity. ...

Class II: Slight limitation of physical activity. ...

Class III: Marked limitation of physical activity. ...

Class IV: Symptoms occur even at rest; discomfort with any physical activity.

Effect of pregnancy on heart disease

- ❖ Worsening of cardiac status

- ❖ CCF, bacterial endocarditis,
- ❖ pulmonary edema,
- ❖ pulmonary embolism,
- ❖ rupture of aneuryism
- ❖ No long term effect on basic defect
- ❖ Abortion
- ❖ Preterm labour
- ❖ FGR
- ❖ Intrauterine fetal demise
- ❖ Congenital heart disease in baby– 3-50% risk depending on the specific lesion in the mother

Management

Team Approach- **Cardio-obstetric team or Pregnancy Heart Team**

- Obstetrician
- Cardiologist
- Anesthetist
- Neonatologist
- CTV surgeon
- Nursing Staff

Termination advised in early pregnancy only:

- Primary pulmonary Ht,
- Eisenmenger syndrome,
- Coarctation of aorta,
- Marfan syndrome with dilated aortic root >4cm
- Dilated cardiomyopathy with impaired LV function

Only in 1st trim, better before 8 weeks, after 12wks termination may be as dangerous as continuing

Suction evacuation preferred (because of greater need of unanticipated operative evacuation)

Antenatal care

Clear counselling of risk and prognosis

ANC every 2 weeks upto 30 weeks then weekly

On each visit note- cough, dyspnea, fever

- Check for -pulse rate, BP, JVP, RR, weight gain, anemia, auscultate lung bases, re-evaluate functional grade,
- Ensure treatment compliance
- Exclude fetal congenital anomaly by level-III USG and fetal ECHO at 20 weeks in maternal congenital heart disease
- Fetal assessment of growth should be monitored clinically and by USG when required

Special Advice

- ✓ Avoid excess work and stress
- ✓ Diet/ Iron and vitamins
- ✓ Hygiene, dental care to prevent any infection
- ✓ Dietary salt restriction (4-6g/d)
- ✓ Avoid smoking, drugs – betamimetics
- ✓ Early diagnosis and treatment of PIH, infections

Therapeutic/prophylactic cardiac interventions as applicable- (Cardiologist)

Women with RHD should receive penicillin prophylaxis

-Benzathine Penicillin 1.2 mega units IM after sensitivity testing every 3 weeks throughout pregnancy

-Diuretics, Beta Blockers, Digitalis, Anticoagulants -Surgical treatment as applicable - balloon mitral valvotomy

Labor and Delivery

- Institutional delivery
- Vaginal delivery is the safest mode of delivery
- Most patients get into labor spontaneously
- In women with mechanical valve switched to heparin, a planned delivery might be more appropriate

Induction of Labor -Only for obstetric indications

In absence of spontaneous onset of labor induction **of labor at 39- 40 weeks** of gestation in all women with stable cardiac disease

Both misoprostol [25 micro gm, prostaglandin E1 (PGE1)] or dinoprostone [1–3 mg or slow-release formulation of 10 mg (PGE2)] can be used safely to induce labor.

Mechanical methods such as Intracervical foley instillation,

Artificial rupture of membranes and infusion of oxytocin can be used safely in women with heart disease.

Oxytocin -Higher concentration with restricted fluid

Use double strength oxytocin but halve rate to reduce total volume of fluids given

Indications for LSCS

Mainly obstetrical

Cardiac Indications of CS

- ✓ Coarctation of aorta-to prevent rupture of the aorta or mycotic cerebral aneurysm
- ✓ Marfan syndrome with dilated root of aorta(>40mm)
- ✓ Aortic dissection or aneurysm
- ✓ Recent myocardial infarction
- ✓ Severe symptomatic aortic stenosis
- ✓ Patients presenting in labor on oral anticoagulants (OACs) in order to protect the fetus from hemorrhagic complications

Contraceptive Advice

- Progesterone – good option- DMPA 3 monthly, Norplant, POPs
- Levonorgestrol IUD –safest and most effective option
- The newer, smaller levonorgestrel-based intrauterine devices are easier to insert, reducing the risk of pain and therefore vasovagal response.
- IUCD- Current WHO eligibility criteria recommend its use (category 2)
- COC - contraindicated because of estrogen component have greatest risk of thrombosis
- Contraception- Barrier,
- Sterilization- vasectomy-best
- Tubal ligation - Interval

CHAPTER-5

PREMATURE RUPTURE OF MEMBRANE (PROM)

Author : Prof. Pushpa Lata Sankhwar

Definition

- Preterm Pre-labor rupture of membranes (PPROM) is rupture of the membranes (bag of waters) any time after 20 weeks of gestation & before 37 weeks gestation but before the onset of labor
- Term Pre-labor rupture of membranes is rupture of membranes after 37 weeks but before onset of labor.

Diagnosis

- History of leaking PV before 37 weeks of gestation
- On P/S examination amniotic fluid may be seen coming out of the cervix or fluid comes out on coughing
- A sterile pad placed over the vulva & examined after an hour may show the pad soaked with amniotic fluid
- Litmus paper test by putting a drop of fluid on pink litmus paper which turns blue in presence of amniotic fluid due to a higher pH. The test maybe falsely positive in presence of blood, infection or semen.

Remember

- If a woman complains of bleeding after 20 weeks of gestation, DO NOT performs a digital vaginal examination.
- A P/V in no way helps to establish the diagnosis of PROM. Instead it may add to the complication by way of introducing infection.

Symptoms & signs typically present	Symptoms & signs sometimes present	Probable diagnosis
Watery vaginal discharge	✓ Sudden gush or intermittent leaking of fluid ✓ Fluid seen at introitus ✓ No contractions within 1 hour	PROM
▪ Foul-smelling watery vaginal discharge after 20 weeks of gestation ▪ Fever/chills ▪ Abdominal pain	✓ History of loss of fluid ✓ Tender uterus ✓ Rapid foetal heart rate ✓ Light vaginal bleeding	Amnionitis
▪ Foul-smelling vaginal discharge ▪ No history of loss of fluid	✓ Itching ✓ Frothy/curdy discharge ✓ Dysuria ✓ Abdominal pain	Vaginitis/cervicitis
Bloody vaginal discharge	✓ Abdominal pain ✓ Loss of foetal movements ✓ Heavy, prolonged vaginal bleeding	Antepartum haemorrhage
Blood stained mucus or watery vaginal discharge	✓ Cervical dilatation & effacement ✓ Contractions	Possible labour (May be term or preterm)

Management

- If vaginal bleeding is present with pain in abdomen: Suspect Abruptio placentae & manage accordingly
- Assess for infection & gestation age
- If pregnancy is < 24 weeks gestation then no role of conservative management & pregnancy is to be terminated. Refer to center with gynecologist for termination
- If no s/s of infection & GA < 34 weeks manage conservatively
- If no s/s of infection & GA ≥ 34 weeks, start prophylactic antibiotics & deliver
- If signs of infection present at any gestational age – diagnose chorioamnionitis, give triple antibiotics (Ampicillin, Metronidazole & Gentamycin) and deliver

Conservative Managements if Pregnancy < 34 weeks but > 24 weeks

- Hospitalize & keep under strict observation
- Ideally refer to facility where NICU/ SNCU available
- Start prophylactic antibiotics
    - ✓ IV ampicillin [2 g every 6 hours] and oral erythromycin [250 mg every 6 hours] for 48 hours followed by
    - ✓ Oral amoxicillin [250 mg every 8 hours] and erythromycin [250 mg every 8 hours] continued for 7 days
    - ✓ Do not give the amoxicillin clavulanic acid combination as it increases chances of necrotizing enterocolitis in the newborn.

- Give corticosteroids for fetal lung maturity
    - ✓ Inj Dexamethasone 6 mg IM 4 doses 12 hrs. apart(preferred)

      OR
    - ✓ Inj. Betamethasone 12 mg IM 2 doses 24 hrs apart
- In cases presenting between 24 to 33 weeks it is recommended to give 4g magnesium sulphate 20% solution slow intravenous over 20 min followed by 1g/hour for 12-24 hours to decrease chances of cerebral palsy in the offspring
- **Monitor for**
    - ✓ S/S of chorio-amnionitis
    - ✓ Placental abruption
    - ✓ Fetal growth & well being

If Chorio- Amnionitis

Present Symptoms & Signs

- **Maternal:**
    - ➢ Fever
    - ➢ Lower abdominal pain
    - ➢ Foul smelling vaginal discharge
    - ➢ Tachycardia
    - ➢ Uterine tenderness
    - ➢ Hot vagina
    - ➢ Leukocytosis
- **Fetal:** Tachycardia

Management

- Start antibiotics
    - Ampicillin
    - Gentamycin
    - Metronidazole
- Deliver immediately irrespective of period of gestation
- Do not give corticosteriods in presence of frank infection
- Do not give Tocolytics

Deliver if

- Woman goes in labour
- Signs of Chorio-amnionitis appear
- Placental abruption
- Fetal distress
- Pregnancy ≥ 34 weeks
- Gross fetal congenital malformation
- Intrauterine fetal death

Mode of Delivery

- Assess cervix
- If cervix favorable – induce & deliver under antibiotic cover

- If cervix unfavorable – ripen cervix & induce if facility for C-sec is available.
- If no signs of infection after delivery, discontinue antibiotics
- If signs of infection present after delivery, continue antibiotic accordingly

Remember

- Remember cord can be torn easily from placenta in preterm labor
- Antibiotics for GBS coverage during labor to be given again
- Delayed cord clamping
- Sepsis, hyperbilirubinemia, hypothermia, hypoglycemia are most important causes of neonatal morbidity and mortality

Key Points to Remember

- Diagnose PROM (Preterm Rupture OF Membrane) and PPROM (Preterm Pre-Labor Rupture of Membranes)
- Identify S/S of Infection
- If leaking, do P/S only to confirm. Don't do P/V.
- If infection, do not give corticosteroids, Tocolytics and Mg So4
- Avoid administering combination of Amoxycillin-Clavulinic acid.

Management

i. Sterile pad to be given to patient.

ii. Antibiotics – IV ampicillin [2 g every 6 hours] and erythromycin [250 mg every 6 hours] for 48 hours followed by oral amoxicillin [250 mg every 8 hours] and erythromycin base [333 mg every 8 hours] continued for 7 days (combination of antibiotics to reduce morbidity caused by infection).

iii. Inj. Dexamethasone 6 mg IM 4 doses 12 hrs. apart (preferred) **OR** Inj. Betamethasone 12 mg IM 2 doses 24 hours apart

iv. Give 4g magnesium sulphate 20% solution slow intravenous over 20 min to decrease chances of cerebral palsy in the offspring (Neuro protection for the fetus)

v. If there are contractions, manage accordingly by giving tocolytics. Tocolytics must be given only for steroid coverage. There is no role of prolonged tocolysis

1. In case patient is being shifted to a higher center, ensure she is stable & Referral form is duly filled with details & time of treatment given.
2. If patient is not being shifted, manage in hospital conservatively with:

   i) Modified bed rest
   ii) Antibiotics
   iii) Corticosteroids for fetal lung maturity
   lv) Magnesium sulphate for neuroprotection
   v) Serial evaluation for symptoms & signs of chorio -amnionitis, labor & placental abruption
   vi) Fetal growth & wellbeing should also be serially assessed
   vii) Pregnancy should be terminated

- If the patient goes into labor
- Signs & symptoms of chorio - amnionitis appear,
- placental abruption ensues,
- fetal distress occurs or
- pregnancy >34 wks
- Grossly congenitally malformed baby
- IUD


राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
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ज्ञानावृते न मुक्तिः

CHAPTER-6

FETAL GROWTH RESTRICTION

Author : Prof. Pushpa Lata Sankhwar

Fetal Growth Restriction (FGR):

- Is pathological condition in which a fetus has not achieved its genetic growth potential, regardless of fetal size.
- Growth restricted fetuses may manifest evidence of fetal compromise (abnormal Doppler studies, reduced liquor volume)

Definition of FGR should include

- CPR ratio
- Uterine artery Doppler
- EFW < 3rd percentile

Types of FGR

Sonographically determined head to abdomen circumferential ratio (HC/AC) used to differentiate growth restricted fetus.

- Symmetrical FGR or type I
- Asymmetrical FGR or type II

CHARACTERISTICS	SYMMETRICAL IUGR	ASYMMETRICAL IUGR
Period of insult	Earlier gestation	Later gestation
Incidence of total IUGR cases	20% to 30%	70% to 80%
Etiology	Genetic disorder or infection intrinsic to foetus	Utero-placental insufficiency
Antenatal scan Head circumference, Abdominal circumference, Biparietal diameter and Femur length	All are proportionally reduced	Abdominal circumference-decreased Biparietal diameter, Head circumference, and femur length- normal
Cell number	Reduced	Normal
Cell size	Normal	Reduced
Ponderal Index	Normal (more than 2)	Low (less than 2)
Postnatal anthropometry Weight, length and head circumference.	Reductions in all parameters	Reduction in weight Length and Head circumference- normal (Brain sparing growth)
Difference between head and chest circumference in term IUGR	Less than 3 cm	More than 3 cm
Features of malnutrition	Less pronounced	More pronounced
Prognosis	Poor	Good

Note: Adapted from Sharma D, Farahbakhsh N, Shastri S, Sharma P. Intrauterine growth restriction–part 2. J Matern Fetal Neonatal Med. 2016 Mar 15:1–12. [Epub ahead of print] PubMed PMID: 26979578 with permission.

ETIOLOGY

EARLY FGR (<32 WKS)

classic concept of defective placentation leading to early-onset FGR

- AC/EFW < 3RD Centile **or**
- AEDF IN UA
- AC/EFW < 10TH Centile with UtA PI > 95TH Centile **and/ or** UA PI > 95th centile

LATE FGR (>= 32 WKS)

Defect in maturational process leading to placental hypoperfusion /diffusion defect

- AC/EFW < 3RD Centile

Or atleast 2 of following

- AC/EFW < 10th Centile
- CPR < 5TH Centile
- UA PI > 95th Centile

Pathology of Asymmetrical FGR

Placental insufficiency

↓

Decreased glucose transfer to the fetus

↓

Decreased hepatic glycogen storage

↓

Decreased size of hepatocytes

↓

Decreased size of liver

↓

Decreased AC

Preferential shunting of oxygen and nutrients to the brain.
Brain and head growth is normal. ⟹ BRAIN SPARING EFFECT
PONDERAL INDEX is low because of low birth weight.

PATHOPHYSIOLOGY

- Reduced availability of nutrients in mother
- Reduced transfer by placenta to fetus
- Reduced utilisation by fetus

Liver glycogen content is reduced

- Renal and pulmonary contribution to amniotic fluid is diminished due to reduced blood flow→Oligohydramnios
- Risk of intrauterine hypoxia and acidosis →death if severe

ETIOLOGY

Maternal

Constitutional

- Small women, maternal genetic and racial background are not at increased risk

- Pre-pregnancy weight less than **100 pounds (<45kg)** or BMI <20 have two-fold risk.
- Reduced intrauterine growth of the mother is a risk factor

Maternal nutrition

- Poor weight gain throughout pregnancy may be associated with FGR.
- Glucose, amino acids and oxygen are deficient during pregnancy which may increase risk.

ETIIOLOGY

1. Maternal

Maternal diseases

- Pre gestational diabetes mellitus
- Hypertensive disease of pregnancy (HDP)
- Renal insufficiency
- Cyanotic heart disease
- Maternal Infection
- Autoimmune disease (SLE)
- Anti-phospholipid antibodies

Social Deprivation

effects of associated lifestyle factors such as smoking alcohol or other substance abuse, and poor nutrition.

Teratogenic Drugs

Tobacco, Opiates, cocaine, anticonvulsants, antineoplastic drugs

Chronic Hypoxia

- high altitude, maternal cyanotic heart disease
- Poor uterine blood flow to placental site for a long time

(leads to chronic placental insufficiency with inadequate substrate transfer)

Multiple gestation

- Increased frequency of preterm and SGA birth
- Risk in SGA -for twins – **25%**, for triplet and quadruplet – **60%**

Infectious disease (risk of FGR- 5-10%)

- **TORCH** and **malaria**
- **Cytomegalovirus:** *direct cytolysis and loss of functional cells.*
- **Rubella:** *vascular insufficiency by damaging the endothelium* of small vessels, reduces cell division
- Hepatitis A and B, Listeriosis, tuberculosis, and syphilis
- Paradoxically, with syphilis, the placenta is almost always increased in weight and size due to edema and perivascular inflammation

2. Fetal

- ☐ **Structural anomalies** - Cardiovascular, renal
- ☐ **Chromosomal abnormality**
  - Triploidy, aneuploidy, Trisomies (13, 18, 21), Turner's Syndrome
- ☐ **Disorders of bone and cartilage**
  - Osteogenesis imperfecta, Chondrodystrophies
- ☐ **Fetal Infections**
  - TORCH infection, Plasmodium malariae, Treponema

3. Placental

Placental and cord abnormalities:

- Chronic placental abruption
- Extensive infarction
- Chorioangioma
- Marginal/ velamentous insertion of cord
- Placenta previa
- Umbilical artery thrombosis

4. Unknown- 40%

FGR RECOGNITION

History-

- LMP
- POG
- Dating confirmation by earliest scan (Most accurately by first trimester scan)

Clinical

☐ **Abdominal Palpation**

limited accuracy for prediction of FGA

☐ **SFH**

- Closely correlates with gestational age after 24 weeks
- Fairly sensitive (30-80%)
- Serial measurement is important

- **Drawback** – maternal obesity, leiomyoma, multiple pregnancy: USG better modality for screening in these cases

Ultrasonography

(RCOG Green top Guideline) -Fetal AC or EFW <10th centile for gestational age as recommended cut offs for diagnosis of SGA.

Evaluation of pregnancy complicated by FGR

- **Ultrasonography**

  Most common method to evaluate fetal growth is **effective fetal weight**
  calculated using multiple parameters i.e. BPD, HC, AC, FL.

- **Amniotic fluid volume**
  - Association between FGR and oligohydromnios
  - Decreased AFI b/w 24-34 weeks associated with **malformations**
  - In absence of malformation -**Birth weight <3 percentile** is found to be associated with oligohydromniosz
  - Doppler velocimetry

Early changes in placenta based growth restriction detected in peripheral vessels- **umbilical and middle cerebral artery**
Late changes characterized by reversal of **umbilical artery flow and abnormal flow in ductus venosus.**

Absent and reversed diastolic flow in umbilical artery related to **fetal acidosis** and **hypoxia** and **fetal death**

Abnormal umbilical artery Doppler velocimetry combined with estimated fetal weight < 3rd percentile strongly associated with poor obstetrical outcome

ACOG 2015 recommended umbilical artery Doppler velocimetry in the management of fetal growth restriction as an adjunct to standard surveillance technique such as non-stress testing and bio physical profile

Ductus venosus Doppler parameters were cardiovascular factors- reflect myocardial deterioration and academia

Antepartum testing (non-stress test & biophysical profile)

Fetal heart monitoring (CTG)-

- 50% false positive for prediction of adverse outcome
- CTG evaluates STV (Short term variability) of the FHR
- STV of FHR closely correlates with acidosis and severe hypoxia

Biophysical profile

- Calculated by combining ultrasound assessment of fetal tone, respiratory and body movement with AFI and conventional CTG.
- Designed to improve FHR
    - Meta-analysis shows no significant benefit of BPP in high risk pregnancy

Management

(RCOG -2014) Green–top Guideline No. 31

- UA Doppler PI > 95TH centile, No other testing abnormalities → Doppler – 2 Weekly; BPP + CTG – Weekly
- Low MCA PI or CPR → Weekly Doppler + BPP + CTG
- UA Absent end – diastolic flow (AEDF) → Admit , 2 times/ week doppler + BPP + CTG
- UA Reversed end diastolic flow (REDF), Increased DV
  or
  Oligohydramnios (SDP < 2cm) → Admit , 3 times/ week doppler with BPP Daily CTG
- Absent or Reversed DV a - wave → Daily doppler with BPP and CTG in preparation of delivery

CHAPTER-7

ACUTE KIDNEY INJURY IN PREGNANCY

Author : Prof. M L Patel

Introduction

Acute kidney injury (AKI) during pregnancy is a public health problem and is a significant cause of maternal and fetal morbidity and mortality. Pregnancy related Acute Kidney Injury (PRAKI) is a significant contributor to the overall burden of AKI and is responsible for 15% to 20% of AKI in developing countries. In India, PRAKI occurs in 1 in 50 pregnancies and represents up to 20% of all cases of AKI. High mortality is associated with AKI (over 30% in majority of studies). On the other hand, incidence of AKI has sharply declined from 1 per 2000 to 1 in 20,000 pregnancies in developed countries.

Physiologic and Anatomic Changes in Kidney during Pregnancy

Anatomical Changes

Size — Both kidneys increase 1 to 1.5cm in length during pregnancy. Kidney volume increases by up to 30 percent, primarily due to an increase in renal vascular and interstitial volume.

There is physiological hydronephrosis of pregnancy in over 90% of women characterized by dilation of calyces, renal pelvis & ureter.

Physiological Changes

Hemodynamic changes –

The major changes include increased blood volume, decreased systemic vascular resistance, and increased cardiac output. There are increased systemic levels of vasodilators, such as nitric oxide and relaxin, and relative resistance to vasoconstrictors, such as angiotensin II. There is typically a fall in systemic blood pressure, usually reaching a nadir by 20 weeks gestation.

Glomerular filtration rate (GFR) increases by approximately 50%, resulting in a physiologic reduction in serum creatinine in the setting of hyperfiltration.

Renal plasma flow can increase up to 85% in the second trimester of pregnancy.

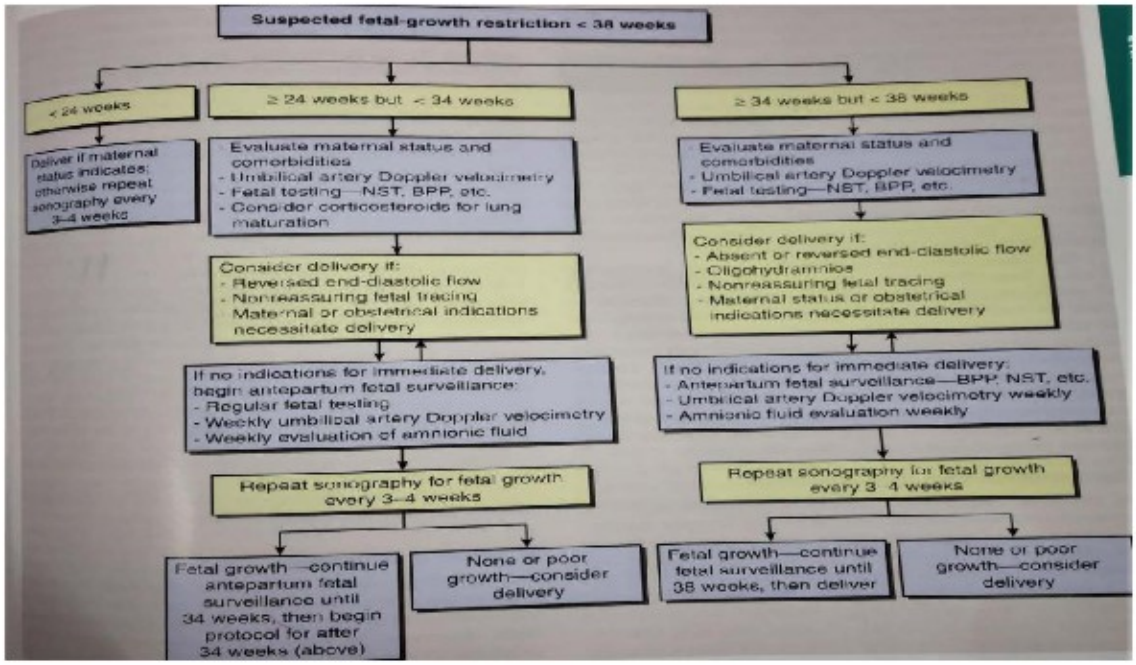
Serum Creatinine- serum creatinine of >77 µmol/l (0.87 mg/dl) should be considered outside the normal range for pregnancy.

Urine protein excretion increases over the course of normal pregnancy, from 60–90 mg/day to 180–250 mg/day, as measured by a 24-hour urine collection. As a consequence of this physiologic increase in proteinuria, the threshold for elevated proteinuria in pregnancy has been set at a higher level of 300 mg/day.

Table 1: Renal changes in pregnancy

Variable	Change in pregnancy
Kidney size	The kidney length increases by 1-1.5 cm and kidney volume increases by up to 30%
Hydronephrosis	Physiological dilation of the urinary collecting system with hydronephrosis in up to 80% of women (right > left)
Renal blood flow	Increased by 80% above baseline
GFR	150-200 ml/min (rise 40-50% above baseline)
Serum creatinine	Falls to 0.4-0.5 mg/dl (*n*=0.8)*
Uric acid	Falls to 2.0-3.0 mg/dl (*n*=4-5)
BUN	Falls to 8-10 mg/dl (*n*=13)*
Sodium	Mild hyponatremia (fall of 4-5 mol/L)
Osmolality	Falls to a new osmotic set point of about 270 mosm/kg

*Considered normal in a nonpregnant individual, reflects renal impairment in pregnant women. BUN: Blood urea nitrogen, GFR: Glomerular filtration rate



Etiology of Acute Kidney Injury in Pregnancy

Usually, the development of AKI during pregnancy follows a bimodal distribution with two incidence peaks: one in the first trimester caused by septic abortion and other in the third trimester and/or around delivery due to late obstetrical complications. AKI is a heterogeneous syndrome in pregnant women and is caused by multiple etiology. It occurs typically in otherwise healthy women who developed obstetrical complication or acquired pregnancy-related medical condition such as PE and/or hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome. However, several etiologies not related to pregnancy (acute gastroenteritis, malaria, pyelonephritis, lupus nephritis, and acute interstitial nephritis) are reported to cause P-AKI. The causes of AKI in pregnant women are divided into three main groups:

obstetrical complications-septic abortion, abruptio placentae, placenta previa, uterine hemorrhage (APH &PPH), Intrauterine fetal demise, Puerperal sepsis

pregnancy-specific disorders- Preeeclampsia, eclampsia, HELLP syndrome, AFLP, Hyperemesis Gravidarum

miscellaneous causes-Acute postinfectious glomerulonephritis,Lupus nephritis,Acute pyelonephritis,dehydration,calculus of urinary tract

As in the general population, the causes of AKI in pregnant women can be divided into three groups: prerenal, intrarenal, and postrenal causes

Age of gestation and clinical presentation are important determinants of AKI in a pregnant woman. We describe below the important causes of AKI during pregnancy.

Causes of AKI in pregnancy	Timing in pregnancy	Signs and symptoms	Cause of AKI	Treatment options
Hyperemesis gravidarum	First trimester	Intractable nausea, vomiting	Volume depletion, possible acute tubular necrosis	Oral hydration, intravenous hydration if necessary
Septic abortion	First trimester	Fever, abdominal pain	Septic acute tubular necrosis	Broad spectrum antibiotics, surgical removal of products of conception
Preeclampsia/eclampsia	After 20 weeks	New onset hypertension (SBP ≥140 mmHg and DBP ≥90 mmHg) and proteinuria	Endothelial damage, coagulopathy/thrombotic microangiopathy, possible acute tubular necrosis	Supportive care, delivery when able, expectant management for preterm pregnancies

Urinary tract infection/acute pyelonephritis	More common after 20 weeks	Flank pain, dysuria, fever, chills	Prerenal AKI secondary to infection, possible acute tubular necrosis	Directed antibiotic therapy
HELLP syndrome	Late second or third trimester	Hemolysis, elevated liver enzymes, low platelets. Can be seen concomitantly with preeclampsia	Endothelial damage, coagulopathy /thrombotic microangiopathy, possible acute tubular necrosis	Delivery when able, imaging for right upper quadrant to rule out hepatic bleeding, hypertension control if severe
Thrombotic thrombocytopenic purpura (TTP)/hemolytic uremic syndrome (HUS)	Usually late second trimester or third trimester for TTP, commonly postpartum for HUS	Hemolytic anemia, thrombocytopenia, neurologic abnormalities	Thrombotic microangiopathy	Plasma exchange +/– rituximab
Acute fatty liver disease of pregnancy	Third trimester	Nonspecific-nausea, vomiting, abdominal pain, hypoglycemia, elevated liver enzymes	Prerenal AKI, possible hepatorenal syndrome appearing picture	Delivery when able, liver transplant if warranted

Lupus nephritis	Delay in pregnancy recommended after 6 months of disease quiescence, kidney manifestations more common postpartum, extrarenal manifestations are more common in second and third trimester	Lupus flare diagnosed with markers of disease activity such as low complement levels, presence of double stranded DNA, and proteinuria	Increased disease activity worsening kidney function	Immunosuppression, continue hydroxychloroquine during pregnancy
Obstructive uropathy	Second and third trimester	Worsening abdominal pain, oliguria	Reflux and obstruction can cause hydronephrosis	Analgesics, increase in fluid intake, stent or percutaneous nephrostomy tube if conservative management unsuccessful
Placental abruption and placental hemorrhage	Third trimester	Increased vaginal bleeding, abdominal pain	Can cause renal cortical necrosis (rare), prerenal AKI from acute blood loss anemia	Control bleeding, supportive care, delivery of infant

Postpartum non-steroidal anti-inflammatory drugs (NSAIDs) use	Postpartum	No specific symptoms, elevated creatinine and band urine analysis	Worsening prerenal AKI in setting of hypovolemia and NSAIDs induced vasoconstriction	Stop NSAIDs, increase hydration, supportive care

Diagnosis of AKI in Pregnancy

The criteria for the diagnosis of AKI in pregnancy have not been standardized. Serum creatinine is typically lower in pregnancy due to hyperfiltration. There are currently no distinct criteria for the diagnosis of AKI in pregnancy, though it is possible that smaller increases in S.cr (less than 0.3 mg/dl) may be more sensitive for picking up early injury.

The Kidney Disease Improving Global Outcomes (KDIGO) definition and staging system is the most recent and preferred definition.

According to **KDIGO 2012 guidelines, AKI** is defined as any one of the following:

1) Increase in S.Creatinine by ≥ 0.3 mg/dl (≥ 26.5 lmol/l) within 48 hours; **or**
2) Increase in S.Creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; **or**
3) Urine volume < 0.5 ml/kg/h for 6 hours.

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ≥ 0.3 mg/dl (≥ 26.5 µmol/l) increase	< 0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	< 0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl (≥ 353.6 µmol/l) OR Initiation of renal replacement therapy OR, In patients < 18 years, decrease in eGFR to < 35 ml/min per 1.73 m^2	< 0.3 ml/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours

Other criteria used to define and stratify the severity of acute kidney injury (AKI) include the RIFLE criteria (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) and a subsequent modification proposed by the Acute Kidney Injury Network (AKIN).

Treatment of Acute Kidney Injury in Pregnancy

The management of P-AKI includes three considerations:

(i) supportive measures to preserve renal function,

(ii) dialysis, and

(iii) treatment of the underlying pregnancy-specific disease.

(I) Renal function supportive measures

The important general measures to minimize renal injury (such as treatment of etiology, avoidance of nephrotoxic drugs or treatment of an infectious disease) should be started as soon as possible.

The second step is administration of intravenous fluids to restore or maintain renal perfusion This procedure also prevents hypovolemia and ensures an adequate uteroplacental perfusion and fetal well-being.

Pharmacological therapy of AKI and its known complications such as hypertension, hyperkalemia, metabolic acidosis, and anemia. Angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists are contraindicated in pregnancy and diuretics are not recommended because of the high risk of volume depletion. The first-line treatment options in pregnant women with hypertension are methyldopa and labetalol. The administration of insulin, glucose, and ion exchange resin is recommended for the treatment of hyperkalemia.

The erythropoiesis-stimulating agent is safe in pregnancy, but higher doses are usually required to obtain the desired therapeutic effect in pregnant women.

(II) Dialysis

The indications for dialysis in P-AKI are similar to the general population, and they include uremic symptoms (encephalopathy, pericarditis, or neuropathy), volume overload, hyperkalemia, and/or metabolic acidosis unresponsive to initial medical treatment. However, early start of dialysis is recommended when GFR falls to below 20 ml/min/1.73 m^2. The intermittent hemodialysis is preferred and dialysis of choice in most patients. It is essential to keep certain aspects in mind when dialysis is prescribed in pregnant women with AKI. They include (i) increased dialysis dose (daily dialysis with duration of more than 20 h/week).

This will improve the uremic environment, a high-risk factor for prematurity and polyhydramnios, and minimize hemodynamic fluctuations of hemodialysis.

(III) Treatment of the underlying pregnancy-specific disease

The specific treatment of AKI depends on the underlying cause of the injury. Treatment of severe preeclampsia, HELLP syndrome and AFLP, require prompt delivery of the fetus. Glucocorticoids are administered if delivery is performed prior to 34 weeks of gestation to decrease the risk of neonatal respiratory distress syndrome.

Treatment of the thrombotic microangiopathies, including TTP, and atypical HUS, includes plasmapheresis and eculizumab (for aHUS). In ADAMTS13-deficient TMA, the goal is to regain enzymatic activity through plasma exchange, and if plasma exchange is unsuccessful, rituximab is an option for treatment. Treatment for glomerulonephritis includes steroid and immunosuppressive therapy, and risk and benefits should be weighted when therapy is initiated in a pregnant woman.

CHAPTER-8

LIVER DISORDERS IN PREGNANCY

Author : Dr. Shalini Singh

Introduction

Hemodynamic, hormonal, and immunological changes during pregnancy alter the course of both acute and chronic liver diseases and also affect the outcome of pregnancy.

High levels of serum estrogen and progesterone affect the metabolic, synthetic, and excretory functions of liver during pregnancy.

Physiological changes in the liver during pregnancy

Increased

- ALP rise 3-4 fold due to placental production
- Fibrinogen rise by 50 %, with other clotting factors
- Cholesterol, triglycerides

Decreased

- Gallbladder contractility
- Serum Albumin and total protein
- Total & free bilirubin

No change

- Liver size
- Liver blood flow (25-35%) despite increased blood volume and cardiac output

- Liver aminotransferase levels, may decrease in third trimester
- Prothrombin time

Liver function Test Includes:

- Serum bilirubin
- Serum AST
- Serum ALT
- Serum ALP
- Serum GGT
- Serum proteins
- Prothrombin time

Rise in ALT & AST- suggests hepatocellular necrosis and increases in ALP & GGT suggests cholestasis

The general rule

- The earlier in pregnancy the liver abnormality presents, the more likely it is to represent either preexisting liver disease or non-pregnancy-related acute liver disease
- Causes of jaundice in pregnancy

Causes unrelated to pregnancy of liver disorders:

Hepatic causes-

- Acute viral hepatitis
- Drug induced hepatitis
- Chronic hepatitis (viral, auto-immune)
- Wilson's Disease

- Cirrhosis of liver
- Budd-Chiari syndrome

Pre-Hepatic Causes

Hemolytic anemia

Post-Hepatic Causes

- Common bile duct stones and
- Strictures Biliary parasitosis

Pregnancy specific causes of liver disorders:

- Hyperemesis gravidarum
- Intrahepatic cholestasis of pregnancy
- Pre-eclampsia/eclampsia
- HELLP syndrome
- Acute fatty liver of pregnancy
- Viral hepatitis
- Prodromal symptoms-fever, anorexia, nausea, vomiting, fatigue, malaise, arthralgia, myalgia, headache

Table 1: Followed by Jaundice, Dark Urine, Pale Stools
Transaminases are classically elevated

Features	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis E
Virus type	Non-enveloped, RNA	Double stranded DNA	Enveloped single stranded RNA	Non-enveloped, RNA
Incubation period	28 days	30-180 days	7 weeks	2-10 weeks
Route	Faeco-oral	Parenteral/sexual/ vertical	Blood borne/ Vertical	Faeco-oral

Diagnosis	Serology, IgM anti-HAV	Battery of tests	Anti- HCV antibodies	Anti-HEV
Fetal effect	Non- teratogenic	Non-teratogenic	Non-teratogenic	Non- teratogenic
Breast feeding	Not contraindicated	Not contraindicated	Not contraindicated	Not contraindicated
Course in pregnancy	unaltered	unaltered	unaltered	Pregnant women more susceptible, progression to fulminant hepatic failure
Treatment	Supportive	Supportive	Supportive	Supportive
Prevention of neonatal infection	Immunoglobulin	Vaccine & Immunoglobulin	No vaccine & immunoglobulin available yet	No vaccine, but immunoglobulins are available
Chronicity of infection	No	Yes	Yes	No
Risk of hepatocellular carcinoma	No	Yes	Yes	No

Pregnancy-associated liver disease

- Predominant in the third trimester and resolve post- partum
- Maternal and fetal mortality and morbidity prevented by early delivery
- Hyperemesis Gravidarum is a disease of first trimester.

Hyperemesis Gravidarum

- ✓ Occurs in 0.3-2% of all pregnancies
- ✓ Presents with persistent vomiting, leading to dehydration with associated ketosis and weight loss
- ✓ Hormonal peaking of HCG and estradiol probably plays role
- ✓ Mild elevation of transaminase in 50% cases, Bilirubin may rise to 4 mg/dl
- ✓ Amylase elevated in 10%
- ✓ Complications include electrolyte imbalance, esophageal rupture, retinal hemorrhage, renal failure
- ✓ Initial management is conservative
- ✓ The only FDA-approved drug for treating nausea and vomiting in pregnancy is doxylamine/pyridoxine
- ✓ However, antihistamines, antiemetics of the phenothiazine class, and promotility agents (eg metoclopramide) are used
- ✓ In refractory cases, ondansetron and steroids may be considered
- ✓ Intrahepatic cholestasis of pregnancy
- ✓ Occurs in late pregnancy
- ✓ Affects around 1.5-2% of pregnancies
- ✓ Pruritis is the most characteristic manifestation, mainly in palm and soles and occur at night
- ✓ Most do not have jaundice

LFT-

- Features of cholestasis,
- High serum bile acid- >10micromol/l
- Conjugated hyperbilirubinemia
- Modest rise in ALP, GGT

- AST/ALT only mildly elevated
- Synthetic function of liver not affected
- Liver architecture not affected
- Progresses till delivery
- Itching disappears within 24-48 hours postpartum but biochemical abnormalities take weeks to months to resolve
- May recur in subsequent pregnancy (60-70%)
- Fetal risks are greatly increased
    - Intrapartum fetal distress
    - Meconium aspiration
    - Neonatal respiratory distress
    - Still birth

Management

- Relief of pruritis by local application of calamine lotion
- Ursodeoxycholic acid most effective treatment
- Vitamin K reduces bleeding (maternal & fetal)
- Fetal monitoring
- Planned early delivery by 37-38 weeks

Acute Fatty Liver of Pregnancy

- Occurs in third trimester of pregnancy. It has an acute onset & can progress very rapidly
- Uncommon disease with high maternal & perinatal mortality
- More common in twins, first pregnancies and male fetus
- Presents with nausea, vomiting, anorexia and abdominal pain followed by jaundice

- Size of liver is normal
- Moderate elevation of AST & ALT
- Presence of hypoglycemia, prolonged Prothrombin time, absence of thrombocytopenia differentiates from HELLP
- Fulminant hepatic failure in severe cases
- Defect in beta-oxidation of fatty acids in mitochondria, leads to fat droplets formation in hepatocyte (microvesicular fatty liver)
- Diagnosis by clinical & lab features
- Early recognition & diagnosis followed by immediate termination of pregnancy along with intensive supportive care is essential for survival

HELLP syndrome

- Acronym for Hemolysis, Elevated liver enzymes, low Platelets
- Occurs in 0.5-0.95 of pregnancies and in 10- 20% of severe pre-eclampsia
- **Clinical symptoms** – upper abdominal pain & tenderness, nausea & vomiting, malaise, headache, edema, weight gain, hypertension & proteinuria
- **Patho-physiology** - activation of coagulation cascade, increase vascular tone, platelet aggregation & an altered thromboxane: prostacyclin ratio. This induce endothelial & microvascular injury leading

Diagnosis-

- low platelet < 1 lac/cumm

- elevated LDH (>600 IU/L)
- AST/ALT (>70 IU/L)

Complications-

MATERNAL - abruption, eclampsia, DIC, ARF, cerebral & Pulmonary edema, liver hemorrhage

FETAL - FGR, placental insufficiency, prematurity, perinatal asphyxia, stillbirth

Management

- supportive
- close monitoring
- delivery is the only definitive treatment
- mild- delivery after fetal maturity
- severe- stabilizing patient & delivery after betamethasone coverage
- Rapid & early resolution occurs after delivery
- Chances of recurrence in subsequent pregnancy

	Acute hepatitis	**Intrahepatic cholestasis**	**HELLP syndrome**	**Acute fatty liver of pregnancy**
Trimester	Any trimester	Third	Third	Third
Presenting symptoms	Fever, jaundice	Pruritis	Hypertension, nausea, vomiting, pain	Nausea, vomiting, abdominal pain
Serum ALT & AST	Markedly high	Normal to mild rise	Moderately high	Moderately high
Serum ALP	Normal to mild rise	High	Normal	Normal

Platelets	Normal	normal	Low	Normal
Fetal complications	Transmission in cases of HBV, HCV	prematurity., fetal distress, IUGR	prematurity, IUGR	Premature delivery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CHAPTER-9

HELLP SYNDROME

Author : Dr. Monica Agarwal

Introduction

Weistein coined the term HELLP, HELLP syndrome is a serious complication in pregnancy

characterized by:

H : Haemolysis
EL: Elevated liver enzymes
LP: Low platelet count

It occurs in 0.5 to 0.9% of all pregnancies and in 10–20% of cases with severe preeclampsia.

In pregnancies complicated by preeclampsia, laboratory findings of HELLP are present in 2% to 20% of cases; in those complicated by eclampsia, HELLP is present in 10% to 30% of cases.

Definition

HELLP syndrome is a severe form of preeclampsia (sometimes called **"atypical preeclampsia"**) characterized by hemolysis (H), elevated liver enzymes (EL), and low platelets (LP) in a pregnant or puerperal patient (usually within 7 days of delivery).

Timing of development

1. Antepartum: 70%

The condition usually occurs antepartum, in 3rd trimester between 27th and 37th weeks gestation

In 10 % cases it occurs in second trimester > 20 weeks

2. Postpartum: 30%
   - It develops mostly within 48 hours of delivery
   - Can develop upto 7 days post delivery

Risk factors

1. Maternal age > 35 years
2. Obesity
3. Chronic hypertension
4. Diabetes mellitus
5. Autoimmune disorders
6. Migraine
7. Abnormal placentation (e.g., molar pregnancy)
8. Previous pregnancy with preeclampsia with/without HELLP syndrome
9. Multiple gestation

Symptoms

1. Nausea, vomiting (29-80 %)
2. Hypertension and proteinuria (80 to 85%)
3. Brisk tendon reflexes
4. Epigastric/right upper quadrant pain (40 to 90 %)
5. Generalised malaise

6. Headache, and malaise. (33-61 %)

7. Edema

8. Visual disturbances (10 -20 %)

9. Jaundice (5 %)

10. Bleeding

Some patients may be asymptomatic

The Triad Signs of Hemolysis, elevated liver enzymes and Thrombocytopenia

Haemolysis, one of the major characteristics of the disorder, is due to a microangiopathic haemolytic anaemia (MAHA). Red cell fragmentation caused by high-velocity passage through damaged endothelium appears to represent the extent of small vessel involvement with intima damage, endothelial dysfunction and fibrin deposition. Presence of fragmented (schizocytes) or contracted red cells with spicula (Burr cells) in the peripheral blood smear reflects the haemolytic process and strongly suggests the development of MAHA. Polychromatic red cells are also seen in blood smears, and increased reticulocyte counts reflect the compensatory release of immature red cells into peripheral blood.

Destruction of red blood cells by haemolysis causes increased serum lactate dehydrogenase (LDH) levels and decreased haemoglobin concentrations Haemoglobinaemia or haemoglobinuria is macroscopically recognizable in about 10% of the women. Liberated haemoglobin is converted to unconjugated bilirubin in the spleen or may be bound in the plasma by haptoglobin.

The haemoglobin-haptoglobin complex is cleared quickly by the liver, leading to low or undetectable haptoglobin levels in the blood, even with moderate hemolysis .

Low haptoglobin concentration (< 1 g/L – < 0.4 g/L) can be used to diagnose haemolysis and is the preferred marker of haemolysis.

Thus, the diagnosis of haemolysis is supported by high LDH concentration and the presence of unconjugated bilirubin, but the demonstration of low or undetectable haptoglobin concentration is a more specific indicator.

Elevation of liver enzymes may reflect the haemolytic process as well as liver involvement.

Haemolysis contributes substantially to the elevated levels of LDH, whereas enhanced asparate aminotransferase (AST) and alanine aminotransferase (ALAT) levels are mostly due to liver injury.

Decreased platelet count in the HELLP syndrome is due to their increased consumption. Platelets are activated, and adhered to damaged vascular endothelial cells, resulting in increased platelet turnover with shorter lifespan.

Diagnosis

HELLP syndrome should be considered in any pregnant person presenting in the second half of gestation or immediately postpartum with significant new-onset epigastric/upper abdominal pain until proven otherwise.

Diagnosis of the complete form of the HELLP syndrome requires the presence of all 3 major components, while partial or incomplete HELLP syndrome consists of only 1 or 2 elements of the triad.

The HELLP syndrome, a serious condition in its complete form, is associated with substantial risk for the mother and her fetus. A wide range of complications may arise and the condition represents diagnostic and therapeutic problems; timing and method of delivery are important.

Main diagnostic criteria of the HELLP syndrome

At present, there are two major definitions for diagnosing the HELLP syndrome.

1. **Tennessee classification**: Sibai proposed strict criteria for "true" or "complete"
2. HELLP syndrome. Intravascular haemolysis is diagnosed by abnormal peripheral blood smear, increased serum bilirubin (≥ 20.5 μmol/L or ≥ 1.2 mg/100 mL) and elevated LDH levels (& gt; 600 units/L (U/L)

2. **Mississippi triple class classification:** proposed by Martin is based on the nadir platelet count any time during the course of the disease. HELLP class Tennessee Classification Mississippi classification

Class 1 Platelets ≤ 100·10 9 /L Platelets ≤ 50·10 9 /L

AST ≥ 70 IU/L AST or ALT ≥ 70 IU/L

LDH ≥ 600 IU/L LDH ≥ 600 IU/L

Class 2 Platelets ≤ 100x10 9 /L

≥ 50x10 9 /L

AST or ALT ≥ 70 IU/L

LDH ≥ 600 IU/L

Class 3 Platelets ≤ 150x10 9 /L

≥ 100x10 9 /L

AST or ALT ≥ 40 IU/L

LDH ≥ 600 IU/L

Laboratory criteria for HELLP syndrome

- Hemolysis, as evidenced by the presence of schistocytes, burr cells, and polychromasia on a peripheral smear. However, peripheral blood smears are not routinely performed in clinical practice, and sufficient evidence of hemolysis can be gained from:
  - ❖ Elevated LDH (> 600 IU/L or twice the upper limit of normal concentration)
  - ❖ Elevated bilirubin (>1.2 mg/dL)
  - ❖ Low serum haptoglobin (rarely performed in practice)
- Elevated liver transaminases: aspartate aminotransferase and/or alanine aminotransferase > 70 IU/L, or twice the upper limit of normal concentration
- Thrombocytopenia: platelets < 100,000/mm³.

Diagnostic Investigations

- CBC with differential including platelets
- Peripheral blood smear
- Liver transaminases
- Bilirubin level

Other investigations:

- Serum glucose level
- Serum creatinine and electrolyte levels
- Antithrombin level
- Haptoglobin level

Differential diagnosis of the HELLP syndrome.

1) Diseases related to pregnancy
   - Benign thrombocytopenia of pregnancy
   - Acute fatty liver of pregnancy (AFLP)

2) Infectious and inflammatory diseases, not specifically related to pregnancy:
   - Viral hepatitis
   - Cholangitis
   - Cholecystitis
   - Upper urinary tract infection
   - Gastritis
   - Gastric ulcer
   - Acute pancreatitis

3) Thrombocytopenia
   - Immunologic thrombocytopenia (ITP)
   - Folate deficiency
   - Systemic lupus erythematosus (SLE)
   - Antiphospholipid syndrome (APS)

4) Rare diseases that may mimic HELLP syndrome
   - Thrombotic thrombocytopenic purpura (TTP)
   - Haemolytic uremic syndrome (HUS)

Management of pregnant women with HELLP syndrome

In general, there are three major options for the management of women with HELLP syndrome. These include:

1) **Gestational age < 24 weeks or 34 weeks:** Primary choice is immediate delivery. The route of delivery should be selected on obstetric indications including cervical status, obstetric history, the maternal and the foetal condition. If the cervix is unfavorable for induction of labour, cervical ripening should be the first step
2) **At 27 to 34 weeks of gestation:** Delivery within 48 hours after evaluation, stabilization of the maternal clinical condition and corticosteroid treatment
3) **< 27 weeks gestation:** Expectant (conservative) management for more than 48–72 hours may be considered

Conservative management (> 48 hours)

Expectant management before completed 34 weeks' gestation may be an acceptable option in selected cases if it is performed in tertiary care units under close maternal and foetal surveillance (e.g. antihypertensive treatment, ultrasound and Doppler examination). Possible advantages due to limited prolongation of pregnancy should be carefully weighed against the increased risks for maternal and foetal complications

Approach towards a woman with a suspect or diagnosed HELLP syndrome

- Clinical maternal status, blood pressure, gestational age (ultrasound determined), signs of labour and bishop score should be determined.

- The laboratory examination must include complete blood cell count, in particular platelet count, coagulation parameters, AST, LDH and haptoglobin and urine examination.
- Ultrasound examination and foetal assessment tests (Cardiotocography and Doppler examination) are important.
- Stabilize the maternal clinical condition with intravenous fluids, antihypertensive drugs (e.g. labetalol or nifedipine) and magnesium sulphate to prevent convulsions
- Monitor closely maternal vital signs and fluid balance

Seizure prophylaxis

If a grand mal convulsion/eclampsia occurs or is likely in the presence of severe headache and hypertension, a continuous infusion of magnesium sulfate should be started

Loading dose: 4-6 g intravenously

Maintenance dose: 1-2 g / hr infusion for at least 24 hours. Magnesium levels should be checked after 4 hours in these patients. If the magnesium level is over 9 mg/dL, the infusion must be stopped and the level rechecked after 2 hours. Infusion can be resumed at a reduced rate when the magnesium level is < 8 mg/dL.

In patients with renal compromise or acute kidney injury, a single bolus of magnesium sulfate can be given without a continuous infusion.

Following delivery, magnesium sulfate administration should continue for 24 hours.

Corticosteroids should be administered for 24 to 48 hours, ideally before delivery is undertaken, in pregnancies < 34 weeks' gestation in order

to enhance fetal lung maturation and diminish risk of intraventricular bleeding and necrotizing enterocolitis.

Antihypertensive therapy

Blood pressure should be monitored every 15 minutes, and if it is at critical levels (≥160/105 mmHg, mean arterial pressure 120 mmHg), immediate reduction is required to a systolic pressure 140-150 mmHg.

Labetalol is commonly recommended for this indication. It can be administered as a continuous infusion, although bolus intravenous administration is more frequently used. If there is no response to the first bolus, incremental repeat doses should be given.

Labetalol: 20 mg intravenously initially followed by 40-80 mg every 10 minutes according to response, maximum 300 mg total dose. Labetalol is contraindicated in patients with asthma or pre-existing cardiac disease, particularly decreased cardiac function. In these patients, nicardipine can be used.

Secondary option

Nifedipine 5mg/hour intravenously initially, increase by 2.5 mg/hour increments every 15 minutes according to response, maximum 10mg /hour

Tertiary option

Hydralazine: 5 mg intravenously every 20-30 minutes according to response

Mode of delivery

Prompt delivery of the fetus and placenta is key to successful management, and virtually all patients will have spontaneous resolution with this management. If the patient is not already in labor, then the choices are induction of labor or

cesarean delivery. The route of delivery should be selected on obstetric indications including cervical status, obstetric history, the maternal and the foetal condition. If the cervix is unfavorable for induction of labour, cervical ripening should be the first step. Cesarean delivery should be performed for the usual obstetric indications.

Attempts to delay delivery more than 48 to 72 hours to maximize fetal benefit are not recommended once the diagnosis is made. The woman should be monitored closely for at least 48 hours after delivery.

Indications for immediate delivery by Caesarean section include:

- Blood pressure > 160/110 mmHg despite treatment with antihypertensive drugs
- Persisting or worsening clinical symptoms
- Deteriorating renal function
- Severe ascites
- Abruptio placentae
- Oliguria
- Pulmonary oedema
- Eclampsia
- Fetal distress

Special conditions

1. With platelet < 25,000 (or < & 30.000 if bleeding or requires surgery)

The effect of the platelet transfusion is only transient as consumption occurs rapidly. One unit of platelets is expected to increase the platelet count by 5000. A standard platelet pack is usually 6 units, estimated to raise the platelet count by 30,000/mm^3.

2. With fibrinogen < 100 mg/dl

Fresh frozen plasma or cryoprecipitate is done. To increase the serum level of fibrinogen by 25 mg, 1g of exogenous fibrinogen has to be administered. This amount is provided by 1 unit of fresh frozen plasma or 6 units of cryoprecipitate. Cryoprecipitate administration is preferable when fluid overload is a concern.

Anesthesia Choice

- Epidural anesthesia is contraindicated if the platelet count is below 75x10 9 /L
- General anesthesia is choice for caesarean section

Management of post-partum HELLP syndrome

- Management is similar to women presenting antepartum
- Antihypertensives
- Magnesium sulphate
- Close monitoring of vitals and fluid intake / output
- Repeated laboratory evaluation

In women with post-partum HELLP syndrome, risk of renal failure and Pulmonary oedema is significantly increased compared to those with an antenatal onset.

Complications

Maternal Complications	Occurrence (percentage %
Eclampsia	4-9
Abruptio placentae	9-20
DIC	5-56

Acute renal failure	7-36
Severe ascites	4-11
Cerebral oedema	1-8
Pulmonary oedema	3-10
Wound hematoma/infection	7-14
Subcapsular liver hematoma	Between 0.9% and <2%
Liver rupture	1.8%
Hepatic infarction	>30 cases combined with APS
Retinal detachment	1
Cerebral infarction	Few case reports
Cerebral Hemorrhage	1.5–40
Maternal death	1–25

Fetal/neonatal complications

- Perinatal death 7.4–34
- IUGR 38–61
- Preterm delivery 4 70 (15% < 28 gestational weeks)
- Neonatal thrombocytopenia 15–50
- RDS 5.7–40

Recurrence risk

- Risk of recurrence is 2-6 %
- Women with h/o HELLP are at high risk for developing preeclampsia in a subsequent pregnancy.


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CHAPTER-10

INTRAHEPATIC CHOLESTASIS OF PREGNANCY

Author : Prof. Rekha Sachan

Introduction

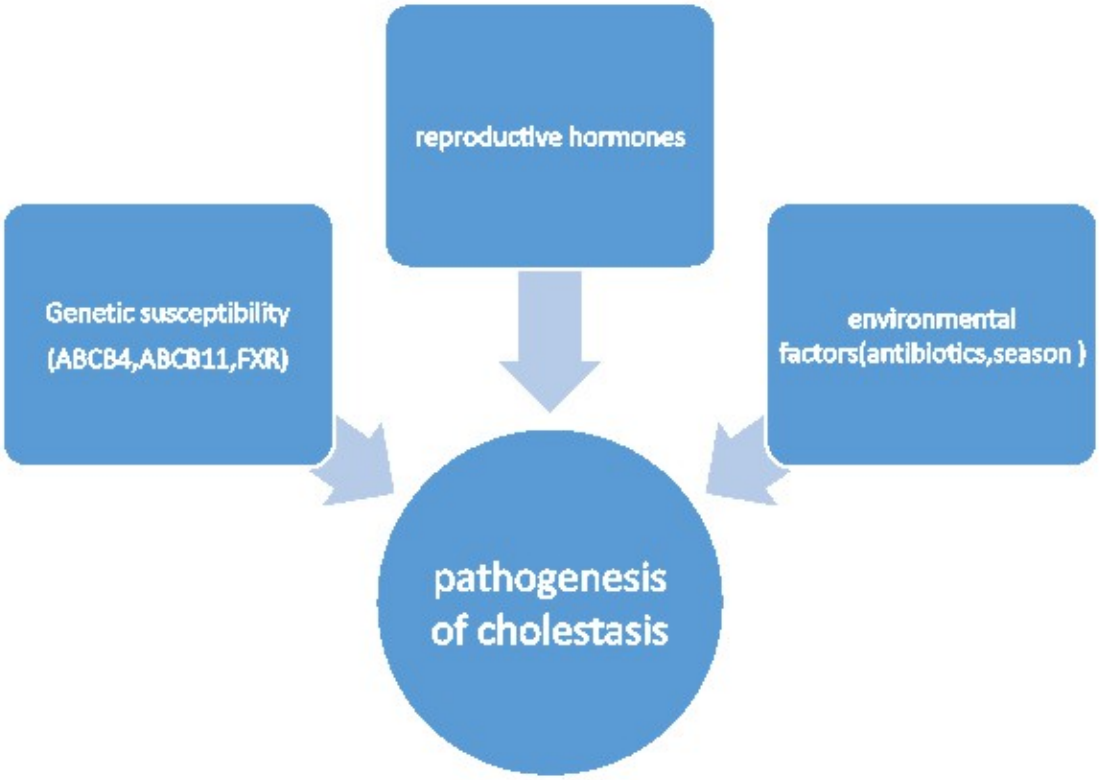
A multifactorial condition of pregnancy characterized by pruritis in absence of skin rash and abnormal liver function tests(LFTs), and both of which resolve after birth.

A number of factors are believed to be involved in decreasing the ability of pregnant women to remove bile acids from their body.

Usually occurs in **third** trimester of pregnancy.

Second most common cause of jaundice in pregnancy after hepatitis.

Prevalence of cholestasis in pregnancy in India is 5% of all pregnancies.



Risk factors

- Personal or family history of cholestasis in pregnancy
- Multiple pregnancy
- Carriage of Hepatitis C
- Presence of gallstones

Clinical presentations

Unexplained pruritis which is worse at night and mostly involves palms and soles) and abnormal LFTs and/or Raised bile acids

Laboratory abnormalities

- Unexplained abnormalities in
- Transaminases
- Gamma-glutamyl transferase
- Bile salts >10micromol/L (most sensitive and specific marker of IHC)

- Alkaline phosphatase is not specific and thereby does not reflect liver disease
- Bilirubin may be raised

Other causes of pruritis and derranged LFTs should be ruled out such as -

- Viral screen for hepatitis A, B,C,EBV,CMV
- Primary biliary cirrhosis by liver ultrasound
- Pre-eclampsia and fatty liver of pregnancy

Fetal risk factors

- Preterm birth (spontaneous 4-12% and iatrogenic upto 25%)
- Meconium passage
- Stillbirth
- Perinatal mortality

Monitoring

- Measure LFTs weekly untill delivery
- If LFT return to normal this rules out the diagnosis of cholestasis
- BP monitoring and tests to rule out other differential diagnosis
- Antihistaminics like chlorpheniramine is used in IHCP to alleviate pruritis.
- Immediate treatment with **ursodeoxycholic acid (udca)** -the drug of choice for treatment og IHCP.
- Initial starting dose is 300 mg BD and can be increased to 300 mg TDS until delivery.
- mechanism of action is unknown, but studies have shown a significant reduction in total bile acids.

UDCA is well tolerated although some of the common side effects are -

- Nausea, vomiting, diarrhea
- If no improvement of IHCP, refractory to UDCA, other medicatiobns that can be used are-

  - ✓ **Rifampicin -** increases bile acid detoxification and excretion
  - ✓ **Cholestyramine -** is anion exchange resin that decreases ileal absorbtion of bile salts thereby decreasing fetal excretion.
  - ✓ **S** - adenosyl methionine

Timing of delivery

RCOG recommends induction of labour after 37+0 weeks of gestation

ACOG recommends delivery between 36+0 to 37 +0 weeks of pregnancy.

Delivery should probably occur by 35 weeks to 36 weeks of gestation if total

bile acid $\geq$ 100micromol/L

Follow-up

Post-partum monitoring and follow up of bile acids and liver function tests should be done in 4- 6 weeks to ensure resolution. Women with persistently elevated LFTs after 6 to 8 weeks require investigation for other etiology.

CHAPTER-11

HIV IN PREGNANCY

Author : Prof. Rekha Sachan

Introduction

Human immunodeficiency virus is a RNA Retrovirus

Types of HIV virus

HIV 1-India

HIV 2-more in Africa, slow & mild in initial stages.

Very fragile Virus

Infects T cells by using CD4 molecule as receptor.

Susceptible to heat, boiling for few seconds kills virus.

1% Na Hypochlorite inactivate virus.

Acquired immune- deficiency syndrome-

AIDS is a syndrome that represents the most severe form of infection with the retrovirus HIV characterized by opportunistic infections, uncommon malignant neoplasms, and neurologic manifestations.

2014 CDC CASE DEFINITION FOR HIV INFECTION AMONG ADOLESCENTS AND ADULTS

STAGE	CD4 COUNT	CD4%	CLINICAL EVIDENCE
STAGE 0	EARLY HIV INFECTION		
STAGE 1	>500 CELLS/MM3	>26	No AIDS defining condition
STAGE 2	200-499 CELLS/MM3	14-25	No AIDS defining condition
STAGE 3	<200 CELLS/MM3	<14	*Or* documentation of AIDS defining condition
STAGE UNKNOWN	NO DATA	NO DATA	No information on presence of any AIDS defining condition

Routes of transmission of virus are-

Sexual Route

Male-to-Female;

Female-to-Male

Male-to-Male

Parenteral Route

Transmission of infected blood

Sharing of infected needles

Parental Route

Mother-to-Child

HIV Virus does not transmit by sharing of towel and toilets and food items, saliva, sweats, tears and by kissing.

Parent to child transmission-

- Known as Vertical or Perinatal Transmission
- Also known as Mother to Child Transmission
- Out of 29 million pregnancies every year, an estimated 22000 occur in HIV infected women.
- 90% of pediatric HIV is due to PTCT
- A total of 61,000 lakh children (0 to 14 years) are estimated to be living with HIV in India

Transmission can occur drug

- Pregnancy
- Labor and delivery
- Breast feeding

Maternal risk factors which affect parent to child transmission of virus

- ☐ High viral load (lower the CD4 count, greater the risk of transmission)
- ☐ HIV subtype (HIV – 2 is less pathogenic)
- ☐ Advanced clinical stage of HIV disease
- ☐ Concurrent STI
- ☐ Viral, bacterial & parasitic placental infection
- ☐ Malnourishment

Obstetrics risk factors affecting parent to child transmission-

- o Uterine manipulations (ECV)
- o Prolonged rupture of membrane >4 hrs
- o Placental disruption (Abruptio, Chorioamnionitis)
- o Intrapartum Haemorrhage
- o Invasive fetal monitoring, scalp blood sampling
- o Invasive delivery techniques (episiotomy, forceps, metal cup in Vacuum delivery)

PPT SERVICES & INTERVENTION

- ❖ Provide HIV information to all pregnant women attending ANC OPD **(Pretest Counseling).**
- ❖ **Voluntary confidential counselling & testing (VCT)** to be given to all pregnant women with an "OPT OUT" option.

Posttest counselling

Counselling the woman to make decision, either to continue or termination of pregnancy

Management of HIV positive women-

- Availability of safe abortion services & sterilization
- Ensure Hospital delivery
- Provide similar antenatal care to HIV positive women as for HIV negativewomen
- Counselling about infant feeding in antenatal period
- Refer to ART center & advice CD4count

WHO STAGING OF HIV INFECTION-

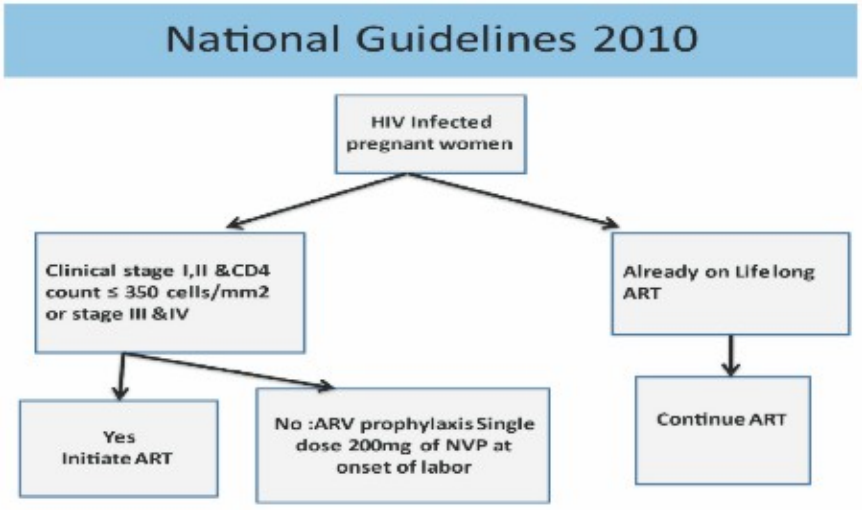
There are four stages according to severity of disease and viral load.

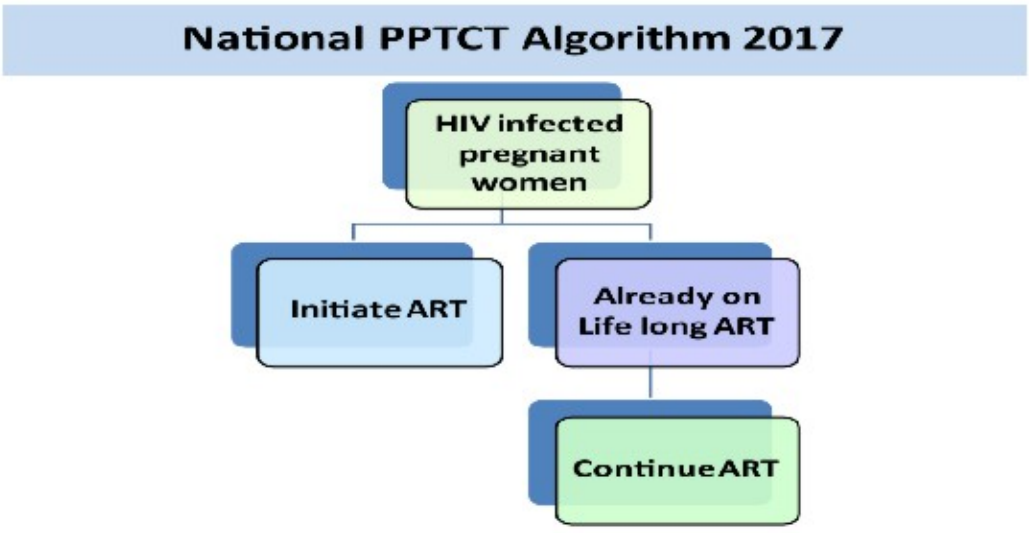
stage 1: asymptomatic

stage 2: mild disease

stage 3: moderate disease

stage 4: advanced immunocompromised state





Initiation of ART in patients living with HIV (PLHIV) with Pregnancy (As per India- PPTCT National guidelines2017)- Regardless of WHO staging should start antiretroviral treatment for life long irrespective of CD 4 Counts

Goal and Objectives of PPTCT Services in India NACO 0CT2018.

Vision: Women and children, alive and free from HIV

Goal: To work towards elimination of pediatric HIV and improve maternal, newborn and child health and survival in the context of HIV infection

Objectives:

1. To detect **more than 90 %** HIV infected pregnant women in India
2. To provide access to comprehensive PPTCT services to **more than 90 %** of the detected pregnant women
3. To provide access to early infant diagnosis to **more than 90 %** HIV exposed infants
4. To ensure access to anti-retroviral drug (ARVs) prophylaxis or Anti-Retroviral Therapy (ART) to **100 %** HIV exposed infants
5. To ensure **more than 95 %** adherence with ART in HIV infected pregnant women and ARV/ ART in exposed children.

Treatment Depends on 4 Points-

1. Pregnant women newly initiating ART
2. Pregnant women already receiving ART
3. ART regimen for pregnant women having prior exposure to NNRTI for PPTCT
4. Women presenting directly-in-labor

1. Pregnant women newly initiating ART

- Start ART as soon as possible after proper counseling and continue ART throughout the pregnancy, delivery, and thereafter life long
- Even if the pregnant women present very late in pregnancy (including those who present after 36 weeks of gestation) the ART should be initiated promptly

This ART shall be initiated at ART centers only, hence all efforts need to be made to ensure that pregnant women reach ART centers.

1) Choice of ART Regimen for HIV positive pregnantwomen

- The recommended first line ART regimen for HIV positive pregnant women

TDF(300mg) + 3TC(300mg) +EFV(600mg)

TENOFOVIR+LAMIVUDINE+EFAVIRENZ

TDF(300mg) + 3TC(300mg) – 1 tab OD +EFV (600mg)

2) Pregnant women already receiving ART

- Pregnant women who are already receiving aNVP- based ART regimen should continue receiving the same ART regimen
- Pregnant women who are already receivingEFV- based ART regimens:

- Should be continued. DO NOT STOP
- There is no indication for abortion/termination of pregnancy in women exposed to EFV in the first trimester of pregnancy.

3)ART regimen for pregnant women having prior exposure to NNRTI for PPTCT

- A small number of HIV-positive pregnant women have had previous exposure to **Single Dose Nevirapine (NVP) for PPTCT** prophylaxis in prior pregnancies
- Because of the risk of resistance to NNRTI drugs in this population, an NNRTI-based ART regimen such as TDF/3TC/EFV may not be effective
- Thus, these women will require a protease inhibitor-based ART regimen.

TDF + 3TC + LPV/r

TDF(300mg) + 3TC(300mg) – 1 tab OD

LPV(Lopinavir) (200mg)/r(Ritonavir) (50mg)———2 tab BD

4) Women presenting directly-in-labour

Women on lifelong ART should continue to receive ART as per the usual schedule including during labour and delivery. Women do not require any other additional ARV dosing

If HIV status not known, then **Whole blood finger prick test should be done-** if test is negative no further test. If test is positive, then give 3 drugs ART & refer to PPTCT Centre for confirmatory test.

Consideration regarding mode of delivery in HIV positive woman-

- In India, normal vaginal delivery is recommended unless the woman has obstetric reasons (like foetal distress, obstructed labor, etc) for a C-section

- Use of ART can reduce risk of PTCT better and with less risk
- Caesarean section should be performed for obstetrical or other medical indication.

Interventions during Labor & Delivery for reducing MTCT

Safe delivery practices should be advocated; these are-

- Vaginal cleaning with 0.25% chlorhexidine
- Minimize cervical examination
- Always use clean technique
- Avoid
  - Routine rupture of membrane
  - Prolonged labor
  - Instrumental deliveries if instrumental delivery is necessary then forceps are better than vacuum
  - Episiotomy, unnecessary trauma during child birth
- Active management of thirdstage.

Interventions for Newborn

- Don't milk the cord
- Cut cord under cover of light gauge
- Do not use suction unless absolutely necessary
- Handle infant with gloves
- Clean injection site with spirit before any injection
- Determine mother's feeding choice before
- Attaching the baby to breast

Intervention for safe feeding practices

Infant feeding as per mother's choice

- Replacement feeding if affordable, safe & sustainable
- Infectious diseases and malnutrition are the primary causes of infant deaths in developing countries. So exclusive breast feeding is recommended for 6 months.
- Avoiding addition of supplements or mixed feeding which enhances HIV transmission

Dose and duration of Infant daily NVP prophylaxis (10 mg of Nevirapine in 1ml suspension)

Infants Birth Weight (gm)	NVP daily dose (mg)	NVP daily dose (ml)	Duration
Birth weight less than 2000 gm	2 mg /kg. once daily In consultation with a pediatrician trained in HIV care	0.2 ml /kg. once daily	Up to 6 weeks* irrespective of exclusive breast feeding or exclusive replacement feeding
Birth weight between 2000 – 2500gm	10 mg. once daily	1 ml once a day	
Birth weight more than 2500 gm	15 mg. once daily	1.5 ml once a day	

*The duration of NVP to infant be minimum 6 weeks but more if ART to mother was started in late pregnancy, during or after delivery (which is less than 4 weeks), then the infant NVP should be increased to 12 weeks.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CHAPTER-12

PLACENTA ACCRETA SPECTRUM

Author : Prof. Rekha Sachan

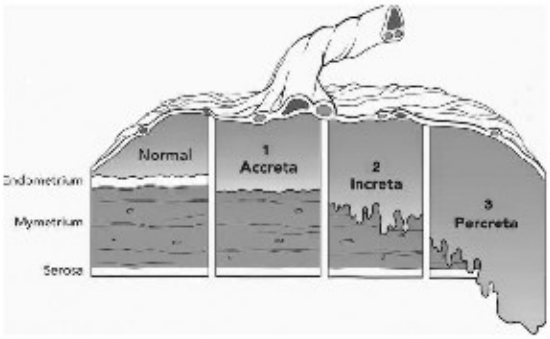
Introduction

- Abnormal trophoblast invasion of part or all of the placenta into the myometrium of the uterine wall.
- Formally known as morbidly adherent placenta

clinical significance

- Life threatening hemorrhage
- Increased maternal morbidity and mortality
- Need for hysterectomy
- Massive blood transfusion
- Surgical injury to bowel and bladder

Grades of placenta accreta spectrum



Risk factors

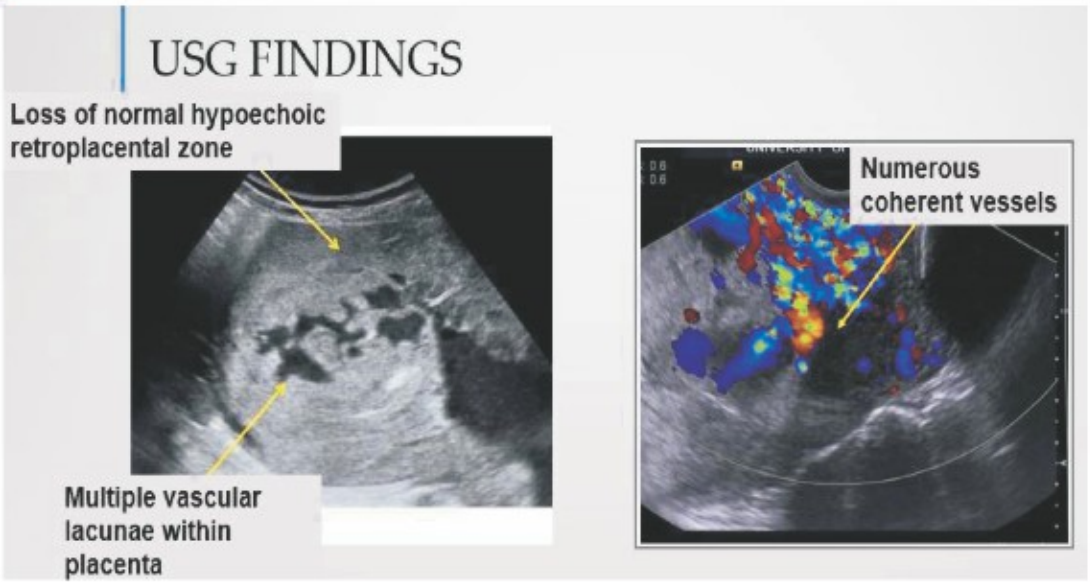
- Previous cesarean delivery with anterior placenta previa
- Previous cesarean delivery
- Placenta previa
- Prior uterine surgery, Asherman syndrome, endometrial ablation
- Multiparity

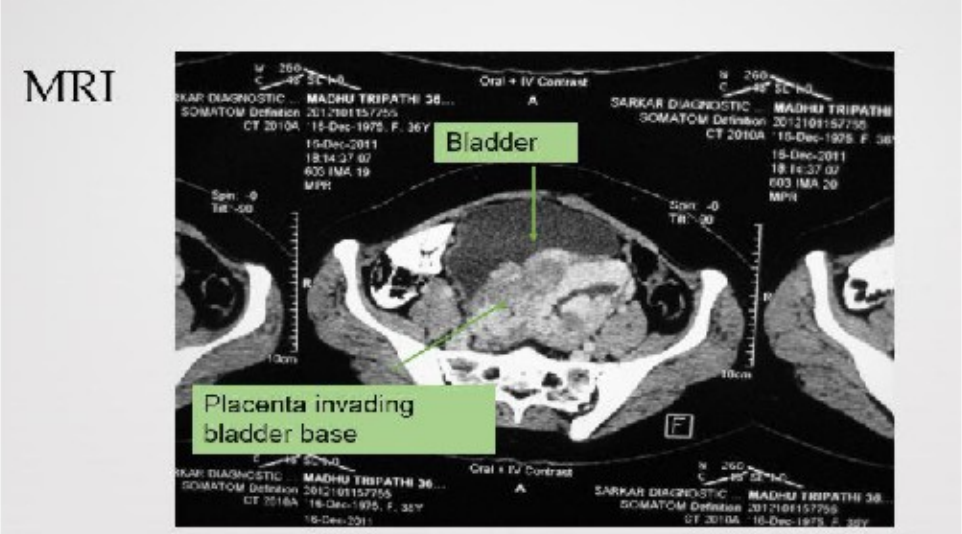
Etiology

- Defect of endometrial-myometrial interface
- Failure of normal decidualization in area of uterine scar.

Diagnosis

1) **Antenatal**
    - Clinical risk assessment
    - Obstetrical ultrasound with colour doppler (sensitivity 90.72%, specificity 96.94%)
    - MRI (sensitivity 94.4%, specificity 84%)
2) Peroperatively- based on uterine appearance (before uterine incision), abnormally adherent placenta





Management of planned placenta accreta spectrum

PREOPERATIVE

- Maximization of hemoglobin
- Specific timing for planned surgery (34 0/7 – 35 6/7 weeks of gestation)
- Necessary preoperative consultations (Multidisciplinary team)
- Relocation to PAS center of excellence
- Bed rest/pelvic rest – unproven benefit
- Early hospitalization – antenatal bleeding, Preterm labour, PPROM
- Ensuring least distance from hospital
- Preoperative ureteric stent placement
- Iliac artery occlusion – routine use not recommended

INTRAOPERATIVE CONSIDERATIONS

- Appropriate surgical expertise
- Availability of related services (interventional radiology)
- Availability of resources (urological equipment, cell-saver)
- Coordination with blood bank

INTRAOPERATIVE MANAGEMENT

- Cesarean Hysterectomy
- Adequate blood products- 1:1:1 (PRBC : FFP : Platelets)
- Autologous cell-saver technology
- Antifibrinolytic therapy (Tranexamic acid)
- Fibrinogen transfusion – efficacy unknown
- Recombinant factor VIIa (positive responses in 76- 86% cases)
- Hypogastric artery embolization
- Pelvic pressure packing, aortic compression or clamping

POSTOPERATIVE

- Assurance of critical care services

INTRAOPERATIVE USE OF TORNIQUETS

- To temporally shut off blood flow through the uterine and ovarian vessels at the level of the uterine cervix.
- Total blood loss in caesarean section and hysterectomy significantly reduced

  Not only prevents massive bleeding, but also allows physicians time to consider the necessity of subsequent hysterectomy

- Patients with placenta accreta are at risk for significant haemorrhage at delivery.
- The key to a successful outcome in these cases is a multidisciplinary approach, appropriate communication, and early planning.

- At our institution, we have assembled an obstetric hemorrhage team that consists of a senior gynecologist, anesthesiologist, and neonatologist.
- After initial case review, an interventional radiologist, urologist, and a blood bank physician are consulted if deemed necessary. Favourable maternal and foetal outcomes have resulted from this team-based approach.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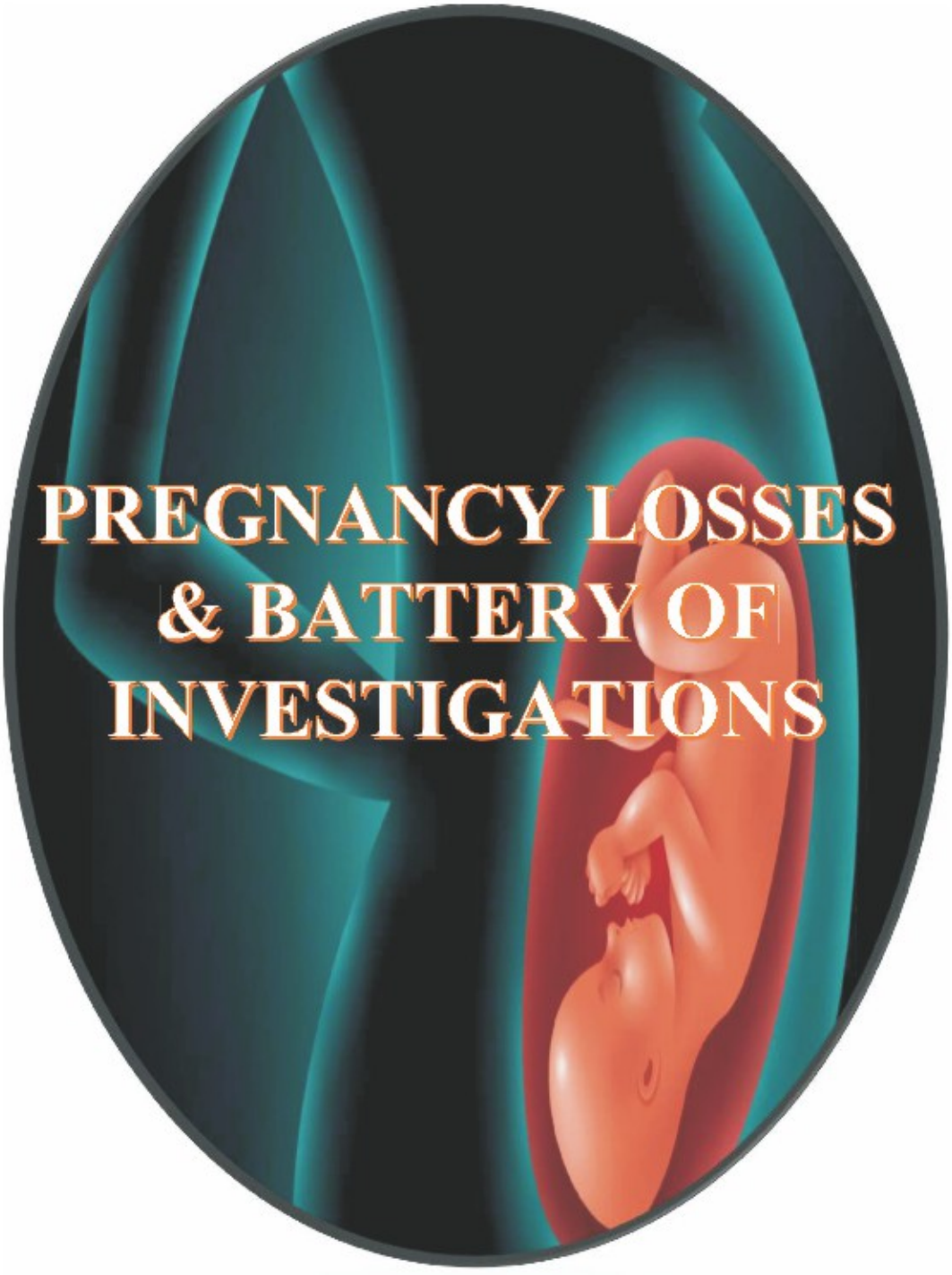
SECTION B

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CHAPTER-1
STILLBIRTH

Author : Prof. Rekha Sachan

Fetal death

Death prior to the complete expulsion of a product of human conception, irrespective of the duration of pregnancy.

Delivery of a fetus showing no signs of life

Absence of breathing, heartbeat, umbilical cord pulsations, definitive voluntary movements

Incidence

> 3 million stillbirths each year worldwide

2020 rate of 9.7/1000 total births in India

Types of Stillbirth

Macerated stillbirth

Fresh stillbirth

Diagnosis of Stillbirth

Absence of fetal movements is the usual symptom

Diagnosis requires real-time ultrasound which should be available at all times. Diagnosis based on absence of fetal heart motion will be wrong up to 20% of the time.Both false positives and false negatives can occur. Scalp clip ECG is a dramatic example. Some mothers feel passive fetal movements. So repeat ultrasound may be required. Colour Doppler may be required in some cases-

- Severe oligohydramnios
- Gross obesity
- Spalding's sign & intrafetal gas sometimes

Etiology

Unknown in 25 – 60% of cases

Identifiable causes can be attributed to

- Maternal conditions
- Fetal conditions
- Placental conditions

Maternal Conditions

- Prolonged pregnancy
- Diabetes (poorly controlled)
- SLE
- APAS
- Infection
- HTN
- Preeclampsia
- Eclampsia
- Hemoglobinopathy
- Rh disease
- Uterine rupture
- Maternal trauma or death
- Inherited thrombophilia

Fetal conditions

- Multiple gestation
- IUGR
- Congenital anomaly
- Genetic abnormality
- Infection
- Hydrops

Placental Conditions

- Cord accident
- Abruption
- PROM
- Vasa previa
- Feto-maternal hemorrhage
- Placental insufficiency

Infection

Most common cause of stillbirth 24 – 27 weeks. It's Contribution to stillbirth rate is difficult to define. Some pathogens are clearly causally related

- Parvo B-19
- CMV
- Toxoplasmosis

Some are associated with stillbirth but absent evidence of causal relationship

- Ureaplasma urealyticum
- Mycoplasma hominis
- GBS

Multiple Gestations

19.6/1,000 stillbirth rate (4x singletons)

Complications specific to multiple gestations

- TTTS
- Increased risk of common complications
- Placental abruption
- Fetal anomalies
- Growth restriction

Advanced Maternal Age

Lethal congenital and chromosomal anomalies

Medical complications associated with age

- Multiple gestations
- HTN
- DM

Unexplained fetal demise is the only type that is statistically more common (late pregnancy)

Obesity (BMI ≥ 30)

Increased risk

- Behavioral, socioeconomic and obstetric factors
- Smoking, diabetes, preeclampsia

Chromosomal Abnormalities

Abnormal karyotype found in 8 – 13% stillbirths. >20% with anatomic abnormalities or growth restriction and 4.6% with normally formed fetuses

Most common abnormalities

- Monosomy X (23%)
- Trisomy 21 (23%)
- Trisomy 18 (21%)
- Trisomy 13 (8%)

Karyotypic analysis underestimates risk

Cord Accidents

Account for only 2.5% of stillbirths in autopsy case series

Attribution requires

- Cord occlusion and hypoxic tissue on autopsy
- Exclusion of other causes

Thrombophilia

Relationship with late fetal death is more consistent than with early losses. They have been associated with late loss but lack of evidence of causal relationship. Thrombophilia's are not uncommon

ReCoDe

Relevant Condition at Death

Group A-Fetus

Group B-UMBILICAL CORD

Group C-PLACENTA

Group D-amniotic fluid

Group E-Uterus

Group F-mother

Group G-Intrapartum

Group H-trauma

Group I-unclassified

Wigglesworth Classification

pathophysiological approach

Category 1: Congenital defect/malformation (lethal or severe):

Category 2: Unexplained antepartum fetal death

Category 3: Death from intrapartum 'asphyxia', 'anoxia or 'trauma'

Category 4: Immaturity

Category 5: Infection

Other specific causes

Category 7: Accident or non-intra partum trauma

Category 8: Sudden infant death, cause unknown

Category 9: Unclassifiable

Pregnancy after stillborn

Early booking & careful dating to be done. Obstetric consultation is must. Screen for gestational diabetes. Monitor fetal growth if previous loss was associated with IUGR. Large studies indicate an increased risk of stillbirth

≈12-fold independent of known recurrent causes

Timing of delivery needs to take into account

- Risks to the baby
- Potential mode of delivery
- The time of the previous fetal loss
- The wishes of the patient

Prevention

- Early prenatal care
- Screen for congenital anomalies
- Optimize health, weight gain
- Reduce multiples
- Improve awareness and management of decreased fetal movement
- Individualize risk assessment late in pregnancy, include race, age, obesity, parity on treating a woman when she is "post-dates"


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CHAPTER-2

RECURRENT PREGNANCY LOSS

Author : Prof. Rekha Sachan

Definition-

≥ 3 consecutive losses of clinically recognized pregnancies < 20 week gestation

Ectopic, molar, and biochemical pregnancies not included

Clinical investigation should be started after two consecutive spontaneous abortions, especially when fetal heart activity had been identified prior to the pregnancy loss or when the women is older than 35 yrs of age or when the couple has had difficulty conceiving

RPL- sub types

- All pregnancy losses, no viable pregnancy
- Viable pregnancy followed by pregnancy losses
- Pregnancy losses interspersed with viable pregnancies

RPL-types

Primary recurrent pregnancy loss" refers to couples that have never had a live birth,

While "Secondary RPL" refers to those who have had repetitive losses following a successful pregnancy

As number of abortion increases the risk of pregnancy loss increases.

	Prior losses	% Risk
Women who have at least 1 live birth	0	12 %
	1	24 %
	2	26 %
	3	32 %
	4	26 %

Risk factors and etiology

- Only in 50 %, the cause can be determined
- Etiological categories:
- Uterine
- Immunologic
- Endocrine
- Genetic
- Thrombophilia
- Environmental

RPL – When To Start Investigating?

Ideally after 3 losses but earlier if high risk patient, elderly, with medical disorders and known family history.

How to Investigate?

Investigate commoner and treatable causes first

Workup

Detailed history – Clarify and Document RPL

- Recurrent Spontaneous. Abortions
- Early Pregnancy Loss Before 8week.s & After 8 weeks
- 2nd Trimester Abortions
- Still Births

Past Obstetric History

Full term birth, premature birth

Malformed fetus

Term of pregnancy at the time of abortion

Location of foetal heart / anembryonic pregnancies

Environmental factors can be diagnosed by history only

- Smoking
- Anesthetic gases
- Toxins, chemicals
- High risk factors – Life Style

Obesity

Daily caffeine intake > 300 mg

Alcohol consumption

Use of NSAIDs

Uterine factors

Acquired or congenital anomalies

Congenital anomalies: 10 -15 %

Abnormal implantation:

↓ vascularity (septum)

↑ inflammation (fibroid)

↓ sensitivity to steroid hormones

Endometrial polyps

Intrauterine adhesions

Cervical insufficiency

Recurrent mid-trimester loss

Other Anomalies

DES exposure (T shaped uterus+/- cervical changes)

Immunologic factors

Autoimmune

(directed to self-tissues /cells)

-Systemic Lupus Erythematosus

-Antiphospholipid Syndrome

Alloimmune (directed to foreign tissues/cells)

An abnormal maternal immune response to fetal or placental antigen.

Endocrine factors

Mild endocrine diseases are likely not causes for recurrent abortion.

1) **Thyroid disease**
2) **Diabetes mellitus**

Poorly controlled (↑Blood glucose & HbA1c levels in 1st trimester) ↑ risk for loss.

3) Polycystic Ovarian Syndrome

Polycystic ovary morphology itself does not predict an increased risk of future pregnancy loss among ovulatory women with a history of recurrent miscarriage who conceive spontaneously (RCOG)

4) Luteal phase defect

1) A defect in Corpus luteum impaired progesterone production.
2) However, LPD cannot be diagnosed during pregnancy; a consistently short luteal phase duration is the most reliable diagnostic criterion.

5) Hyperprolactinemia

Endocrine factors

Thyroid Function Tests- T3, T4, TSH

S.Prolactin

Glucose tolerance test

HbA1c

S.FSH

S. LH

S.Progesterone

Treatment

If there is Luteal-phase insufficiency then- luteal-phase support with progesterone

In case of PCOS, hyperandrogenism, hyperinsullinemia-insulin-sensitizing agents (METFORMIN) overt diabetes mellitus-

prepregnancy glycemic control hypothyroidism-thyroid hormone replacement

Genetic factors

Repetitive first trimester losses

Anembryonic pregnancies

History of malformations or mental retardation

Advanced maternal age

Management

Genetic Councelling

Assisted reproductive technologies, including PGD (preimplantation genetic diagnosis)

use of either donor oocyte or donor sperm depending on the affected partner

Thrombophilia

Thrombosis on maternal side of the placenta and it impairs placental perfusion

Late fetal loss, IUGR, abruption, or PIH

Inherited thrombophilic defects,

including activated protein C resistance (most commonly due to factor V Leiden gene mutation), deficiencies of protein C/S and antithrombin III, hyperhomocystenaemia and prothrombin gene mutation,

☐ are established causes of systemic thrombosis

- ☐ Evaluate if loss > nine weeks + evidence of placental infarction or maternal thrombosis
- ☐ Antithrombin III, Protein C, Protein S, prothrombin gene, factor V Leiden

Antithrombotic Therapy

combined use of low-dose aspirin (75-80mg/dl) and subcutaneous unfractionated heparin (5000 unit twice daily)

Miscellaneous

- Environmental chemicals & stress
- Anesthetic gases (nitrous oxide), formaldehyde, pesticides, lead, mercury
- Personal habits Obesity, smoking, alcohol, and caffeine
- Exercise-does not ↑ sporadic or RPL
- Male factor
- Trend toward repeated miscarriages with abnormal sperm (< 4% normal forms, sperm chromosome aneuploidy)
- Infection-Listeria, Toxoplasma, CMV, and primary genital herpes
- Cause sporadic loss, but not RPL
- Decreased ovarian reserve
- Quality and quantity of oocytes decrease
- Women with unexplained RPL have a higher D3 FSH and E2 than women with known cause

Investigations

Etiology	Investigation
Genetic/Chromosomal	Karyotype both partners
Anatomical	HSG, hysterosonogram, ESI laparoscopy & hysteroscopy,MRI
Endocrine	TSH, prolactin, +/- GTT
Immunological	Anticardiolipin, lupus anticoagulant screen
Thrombophylia	Antithrombin III, Protein C, Protein S, prothrombin gene, factor V leiden
Infectious	Cervical Cultures

Management

1. **Anatomical distortions of the uterine cavity**

   (surgical correction, hysteroscopically, laparotomy)

2. **Control of Endocrinological diseases**

   (control of diabetes, thyroid disease, progesterone luteal support)

3. **Antiphospholipid antibodies**

   (aspirin and heparin)

4. **Thrombophilia**

   (heparin)

CHAPTER-3

ANTIPHOSPHOLIPID SYNDROME

Author : Prof. Rekha Sachan

The anti-phospholipid syndrome (APS) is a systemic autoimmune disorder characterized by recurrent arterial or venous thrombosis and/or recurrent pregnancy loss accompanied by increased titres of antiphospholipid antibodies.

Antiphospholipid antibodies are autoantibodies that are directed against phospholipid-binding proteins. APLA antibodies can be detected in 1-5% of normal population, more so in elderly. Can be induced by inflammation, chronic infection, malignancy, stress and drugs. The most common sites of venous and arterial thrombosis are the lower limbs and the cerebral arterial circulation, respectively. However, thrombosis can occur in any organ.

The three known APLA are:

1. Anticardiolipin antibodies IgG or IgM (ELISA)

2. Anti-beta-2-glycoprotein-I antibodies IgG or IgM (ELISA)

3.lupus anticoagulants (Functional assays)

Diagnosis of APLA Syndrome

First criteria for diagnosis was formulated in post conference workshop in October 1998 at Sapporo, Japan known as Sapporo classification.

Revised criteria published in 2006.

Revised criteria for APLA syndrome

Clinical criteria

Vascular thrombosis

One or more episodes of arterial, venous or small vessel thrombosis in any organ.

Pregnancy morbidity

One or more unexplained loss of morphologically normal fetus >10 weeks of gestation.

One or more premature births before 34 weeks due to pre-eclampsia, eclampsia or placental insufficiency.

Three or more unexplained consecutive spontaneous abortions before 10 weeks with maternal anatomical, hormonal and parental karyotype excluded.

Laborarory criteria

Lupus anticoagulant present in serum on 2 more occasions at least 12 weeks apart detected.

Anti cardiolipin antibody of IgG and/or IgM isotype in serum present in medium to high titer on two or more occasion 12 weeks apart measured by ELISA.

Anti-beta 2 glycoprotein1 antibody of IgG and /or IgM isotype in serum in titre > 90th percentile present on 2 or more occasion 12 weeks apart measured by ELISA.

Mechanism of pregnancy loss

Thrombogenic

Nonthrombogenic

- APLA binds to endothelial cells activates these cells to express adhesive molecules,secrete pro-inflammatory substances and modify PGS metabolism.
- Increase VCAM1, ICAM1 leads to increase monocyte adhesion and thrombosis.
- Increase PAF leads to platelet activation and thrombocytopenia.
- APLA interfere with action of protein C and inhibit protein S and plasminogen.
- Increase synthesis of thromboxane by trophoblast.
- Level of expression of annexin V on intervillous surface and endothelial cells reduced.
- Binding of antibodies to beta2 glycoprotein 1 phospholipid complex leads to dysfunction of beta 2 glycoprotein 1 as a regulator of coagulation.

Non Thrombogenic

- Direct effect of APLA on trophoblast function resulting in direct cellular injuryand inhibition of syncytia formation.
- APLA antibodies inhibit HCG secretion by trophoblast.
- Defective implantation by deficiency of pro-urokinase.
- Interleukin-3 level decreased.
- APLA inhibits PGs synthesis indecidual cells.

Laboratory Testing

Coagulation based assays for lupus anticoagulant

IgG ang IgM Antibody testing for anticardiolipin, beta2 glycoprotein1 by ELISA.

Both tests must be done for the diagnosis of APLA syndrome.

Majority of patients are positive for aCL and LA,about 10-16% are positive for LA only and about 25% are positive for aCL only.

Anticardiolipin Antibodies - detected by ELISA. Clinical manifestation of APS occurs majorly with medium to high levels of aCL. IgG is more prevalent. Results are expressed in semi quantitative terms. Low positive 20 units, medium positive 20-80 units and high positive above 80 units.

Lupus anticoagulant

LA more specific for APLA Syndrome

- LA test measures the ability of APL antibodies to prolong phospholipid dependent clotting reactions.
- 3 sequential steps to establish presence of LA.
- **Step 1** sensitive screening using aPTT, dRVVT, KCT, PT.It is imperative to use 2 screening procedures, if one or both positive then proceed to second step.
- **Step 2** demonstration of an inhibitor, it requires mixing of patient's plasma and normal plasma in various ratios 1:1,1:4 etc.
- In the presence of an inhibitor addition of normal plasma will not result in correction of prolonged screening test.
- **Step 3** demonstration of phospholipid dependence of the inhibitor.

Complications

- Thrombosis

- Can be arterial or venous
- Recurrent pregnancy loss
- Pre-eclampsia, eclampsia and severe eclampsia
- Fetal growth restriction
- Fetal distress

Pre- pregnancy Management

- Presence of clinically significant levels of APLA.
- Counselling regarding thrombosis, gestational HTN, preeclampsia, uteroplacental insufficiency, pregnancy loss, preterm delivery.
- Check for anaemia, thrombocytopenia, KFT.
- Discuss anticoagulation prophylaxsis option and risks of anticoagulation therapy.
- Sometimes low dose aspirin is recommended prior to conception. (8mg/dl)

Management

- ✓ Antenatal management planned for 2 groups of patients
- ✓ Previous thrombotic event
- ✓ Previous pregnancy loss
- ✓ Previous thrombotic event needs anticoagulation in therapeutic doses throughout the pregnancy and at least 6 weeks postpartum.

Previous pregnancy loss

- Both UH or LMWH can be used.

- Warfarin can be used from 14-34 weeks of gestation in patients with previous stroke or arterial thrombosis.
- UH 5000-7500U SC BD for recurrent early pregnancy loss.
- 7500-10000U SC BD in 2nd and 3rd trimester.
- After starting HEPARIN, platelet count should be repeated after 1-2 weeks.

Early pregnancy loss

- Enoxaparin 40mg SC OD or 1mg/kg.
- Dalteparin 5000U SC OD or 200U/kg.

Late pregnancy loss

- Enoxaparin 30mg SC BD
- Dalteparin 5000U SC BD
- Treatment is monitored with aPTT.

  Includes ASPIRIN, CORTICOSTEROIDS, HEPARIN and recently intravenous immunoglobulins. Most accepted is combination of UH/LMWH and low dose ASPIRIN.

- IVIG(immunoglobulin) therapy useful in refractory cases, which fail to respond to heparin.

  Close monitoring and fetal surveillance is recommended due to high risk of pre-eclampsia, fetal growth restriction and placental abruption

- Prenatal visits every 2 weeks until 20-24 weeks and every 1 week after 24 weeks.

- Routine monitoring for pre-eclampsia, uterine artery Doppler in 2nd trimester is useful adjunct in predicting adverse fetal and neonatal outcome.
- Serial USG monitoring every 2 weeks after 18 weeks due to increased risks of IUGR and oligohydramnios
- NST and BPP weekly after 32 weeks.
- Women with APLA syndrome are usually induced at 38-39 weeks.
- Continue fetal monitoring throughout labor.
- Women on WARFARIN should be switched over to heparin at 34 weeks and heparin should stop anytime uterine contractions appears.
- Women at extremely high risk for thromboembolism including those having event within 2 weeks, start IV heparin in labor and discontinued 2-4 hours prior to anticipated delivery.
- IV heparin resumed 4-6 hours after vaginal delivery and 12 hours after cesarean.

Postnatal management

- Prophylaxis to be started 6 hours after vaginal delivery and 12 hours after LSCS.
- Heparin should continue for 6 weeks postnatally.
- Warfarin should be started 2-3 days later and heparin can be discontinued once adequate INR is achieved.
- OCPs are avoided usually due to risk of thrombosis.


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CHAPTER-4

TORCH INFECTION IN PREGNANCY

Author : Prof. Rekha Sachan

TORCH complex is a set of perinatal infection that can lead to severe fetal structural anomalies, developmental defects or even fetal loss.

They are group of viral, bacterial and protozoal infections that gain access to fetal blood stream via transplacental route.

It stands for

T- Toxoplasmosis

R- Rubella

C – cytomegalovirus

H- herpes virus

- Routine "TORCH PANEL" screening is not recommended in low risk asymptomatic pregnant women
- It's not helpful and should not be done for investigation of recurrent miscarriage, since TORCH infections are not responsible for recurrent pregnancy loss.

Indications for maternal TORCH screening during pregnancy

1. Fever, fever with non-vesicular skin rash

2. H/O contact/exposure

3. Lymphadenopathy, unexplained hematological signs/symptoms

4. Ultrasound evidence of markers for congenital TORCH:

- Fetal hydrops
- Fetal brain lesions
- Unexplained IUGR
- Polyhydramnios/Oligohydramnios

Infection		1st trimester	2nd trimester	3rd trimester	Vaginal delivery
Toxoplasma		10-15% (severe)	20-25% (<5% severe)	60-70% (mild symptoms)	-
Rubella	primary	60%(4wks) 25%(5-8ks) 15% (9-12ks)	<5% >20 wks - absent	-	-
	Recurrent	Rare			
CMV	Primary	30-40%			(rare)
	recurrent	0.2-2%			
HSV	Primary recurrent	Rare			40-60% <5%

Timing TORCH infections in relation to the gestational age

- It is important to detect the gestational age when signs of infection noticed and fetal affection detected, since medical termination of pregnancy not permitted beyond 20 weeks.

- Time of infection also directly related to the severity of disease in fetus
- There are two tests that help to time the infection in relation to gestational age

1) Paired serology
2) Avidity testing

Perinatal TORCH transmission and period of gestation at infection

Avidity testing in maternal TORCH infection

- The term **avidity** or **functional affinity** defines the net antigen binding force of populations of antibodies.

Antibodies	Indication	Expectation	treatment
IgM negative IgG negative	No recent infection No past infection	Not immune	If vaccine available can be given
IgM positive IgG negative	Recent infection for the first time	Expect severe sequelae if fetal infection	Treat primary infection if possible
IgM positive	Recent infection + some immunity ?reinfection	Do IgG avidity	Avidity test helps in timing the
IgG positive		Low avidity- recent infection High avidity – old infection	infection

IgM negative IgG positive	Past infection/ immunity	No treatment needed	No vaccine needed

- low avidity is not absolute indicator of recent infection however , high avidity rules out recent infection of less than 4 month , even if IgM is positive

Toxoplasmosis- Can be transmitted in any trimester but maximum chances seen in third trimester. Maximum damage and severity seen if transmitted in first trimester

Clinical features- Most acute maternal infections are subclinical and are detected only by prenatal or newborn serological screening. Maternal symptoms may include fatigue, fever, headache, muscle pain, maculopapular rash and posterior cervical lymphadenopathy. Immunocompetent adult infection confers immunity.

- Immunocompromised individual may develop encephalitis
- Maternal infection is associated with fourfold increase in preterm delivery

Fetal Manifestations-

generalsed - HepatoSpleenomegaly ,↑ liver enzymes (jaundice) , ↓platelet count (petechiac) — TORCH baby

specific to toxoplasma - Hydrocephalous, Diffuse Intracranial Calcification, Chorioretinitis, Epilepsy, Low birth weight

Treatment-

Pregnant women acquired infection before pregnancy- no treatment

Suspected or confirmed acute infection after conception-Spiramycin (3gm/day) till confirmation

Rubella

Maternal Clinical features-25 to 50% infection are asymptomatic, Maternal rubella is usually mild febrile illness with generalized maculopapular rash beginning on face and spreading to trunk and extremities.

Other symptoms- arthralgia, lymphadenopathy, conjunctivitis

The classical triad of defects associated with congenital rubella syndrome-sensorineural deafness (m/c), cataract, heart defect.

Other features- microcephaly, micropthalmia, hepatosplenomegaly , intellectual disability, neonatal purpura and radiolucent bone disease

No specific treatment for rubella, Droplet precaution for 7 days after onset of rash is recommended

Post exposure passive immunization with polyclonal immunoglobulin may be of benefit within 5 days of exposure

MMR vaccine should be given to non- pregnant women of child bearing age

Vaccination should be avoided 1 month before or during pregnancy because vaccine contain attenuated live virus (Plotkin RA 27/3)

MTP should be advised in first trimester

Cytomegalovirus

Most common perinatal infection.

Transmission to fetus- transplacental, intrapartum contact with blood, postpartum- breastfeeding

Symptoms-

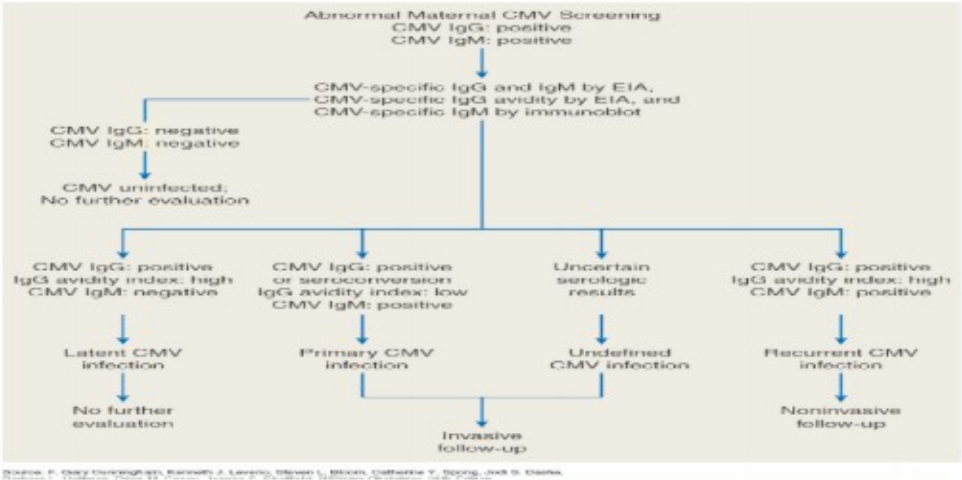
Maternal-mostly infections are asymptomatic

- 10-15 % have mononucleosis like symptoms- Fever, pharyngitis, lymphadenopathy and polyarthritis
- Immunocompromised female may develop- pneumonitis, myocarditis, hepatitis, gastroenteritis, retinitis, meningoencephalitis

Fetal-

Generalized- Hepatosplenomegaly, increase liver enzymes (jaundice), decrease platelet count

Specific to CMV - IUGR, Microcephaly, Periventrcular Calcfication, Micro-ophthalmia, Chorioretinitis, BlueBerryMuffin spots, Mental retardation, sensorineural hearng loss



Management- symptomatic treatment

Herpes Simplex Virus (HSV)

Transmission- 86% = Intrapartum/during delivery ,10% = postpartum, 4% = congenital

Can be transmitted from mother to fetus in both primary genital herpes (40-50%) and in recurrent infection (4-5%).

Clinical feature- Blistering lesions around the vulva and vaginal opening

Risk of transmission increases in:

1) Rupture of membrane for >4hrs

2) Use of scalp electrode for fetal monitoring

Diagnosis- HSV type-specific antibody testing by using enzyme immunoassay

Management- The management of pregnant women with recurrent genital herpes is complex

Main issue is preventing transmission to the neonate during birth.If typical genital lesions are present at delivery, then cesarean section is indicate If transmission already occurred DOC= Acyclovir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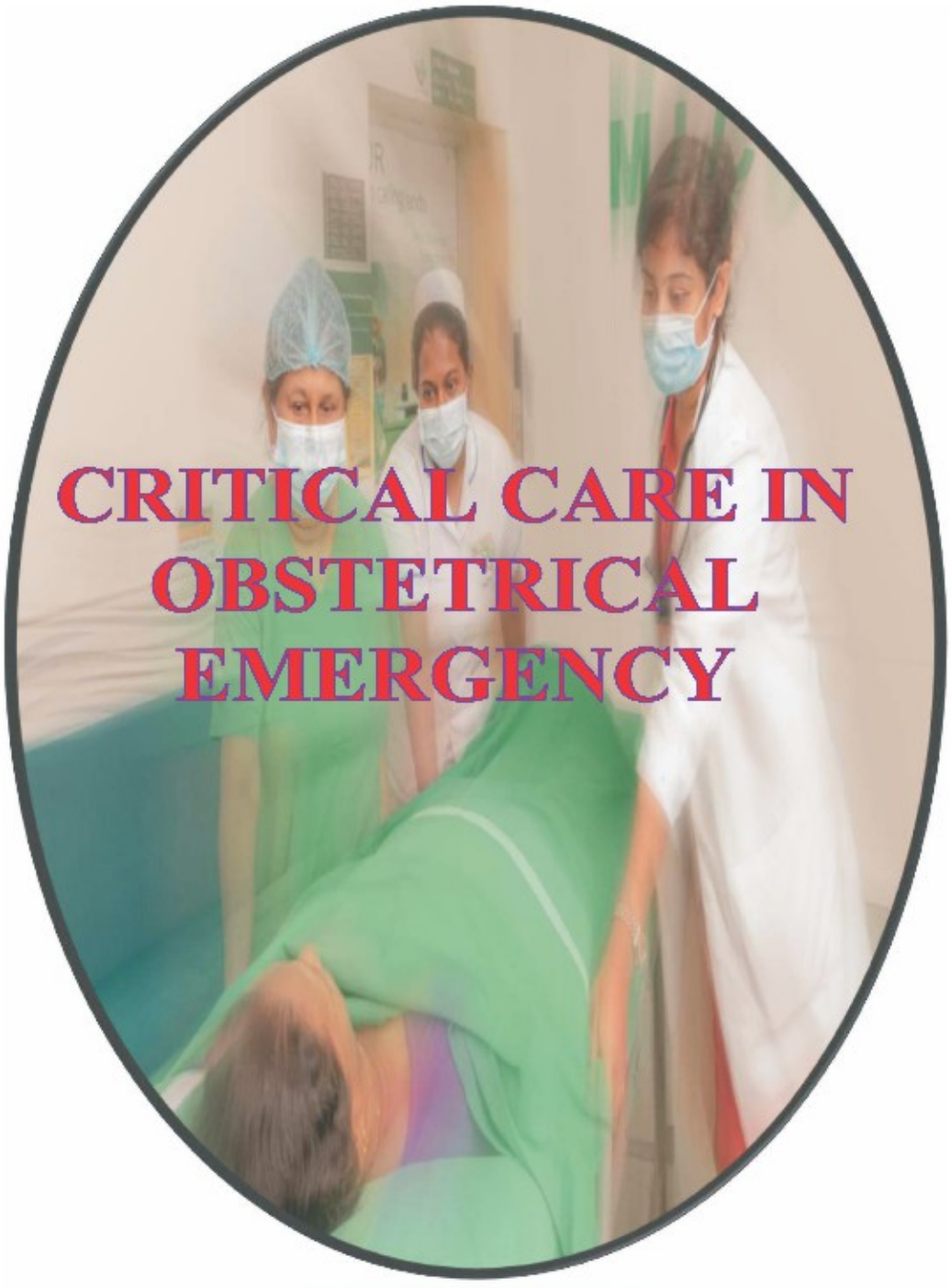

CRITICAL CARE IN OBSTETRICAL EMERGENCY


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CHAPTER-1

RUPTURE UTERUS

Author : Prof. Rekha Sachan

Introduction

- One of the serious cause of maternal and perinatal mortality and morbidity
- Since 1916 the times of Edward Cragin's famous quote,

'Once a Caesarean ,always a caesarean'

Catastrophic uterine rupture

In past 20 yrs VBAC has been encouraged

- Incidence of scar rupture in low transverse incision is 0.2 – 0.9 % and 2-9 % in classical scar
- **Rupture** –Complete disruption of all uterine layers

Prior Incision	Estimated rupture risk (%)
One low transverse	0.2-0.9
Multiple low transverse	0.9-1.8
Low-vertical	1-7
Classical	2-9
T-shaped	4-9
Prior uterine rupture	
Lower segment	2-6
Upper segment	9-32

- **Dehiscence** –Clinically occult uterine disruption. Serosa is intact
- The greatest risk factor for either form of rupture is **Prior caesarean delivery**

Types of prior uterine incision and estimated risk for uterine rupture

Type of Rupture

A) Rupture of Previous Scar

Myomectomy

Hysterotomy

Caesarean Section

B) Rupture of unscarred uterus

Uterine anomalies

Blunt trauma

Internal cephalic version

Prev H/O curettage

Multipara

Instrumental delivery

Risk factors

- Previous uterine rupture
- Previous fundal or high vertical hysterotomy
- Patients with a previous low vertical hysterotomy
- Induction
- Misoprostol – The risk of rupture with use of misoprostol was sufficiently high (approximately 5 to 10 percent
- Oxytocin alone – Induction of labor with oxytocin alone appears to

be associated with only a marginally increased risk for uterine rupture

- Labor – The incidence of rupture is higher in patients who undergo a TOLAC than in women who undergo planned repeat cesarean delivery (PRCD; at term: 0.78 percent with TOLAC and 0.02

Possible risk factors

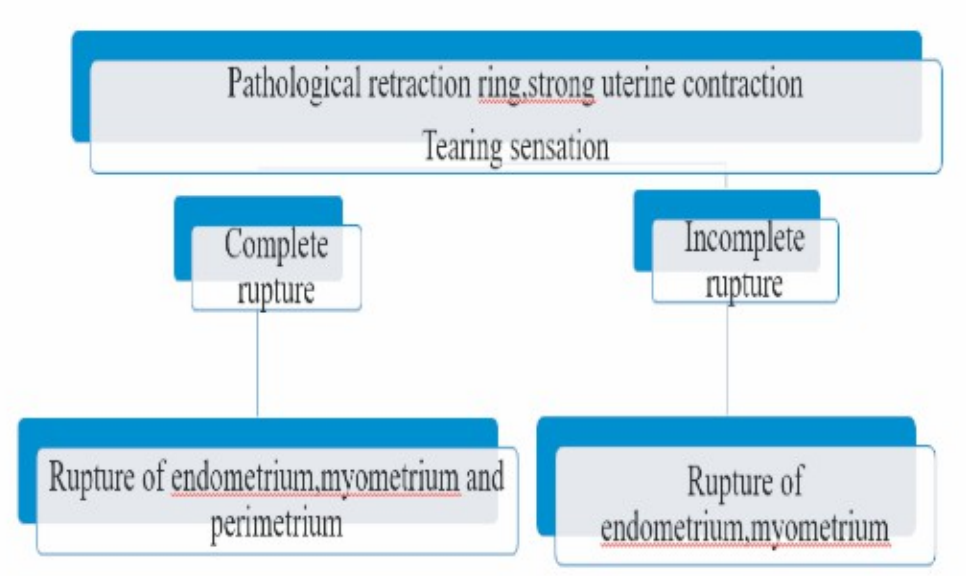
- Increasing maternal age

  Gestational age >40 weeks

  Birth weight >4000 grams

  Inter-delivery interval less than approximately 18 months
- Single-layer uterine closure, especially if locked
- More than one previous cesarean birth Previous second-trimester cesarean birth
- **Factors that decrease the risk of rupture** — A prior vaginal delivery, either before or after the prior cesarean birth

Pathophysiology



Bleeding per vagina and hemoperitoneum

↓

Decrease blood volume, cardiac output

↓

Vasoconstriction of peripheral vessels, Increased heart rate

↓

Decrease perfusion to brain and kidney (loss of consciousness, renal failure)

↓

Decrease uterine perfusion----Fetal distress

Mother and fetus death

Clinical manifestations of uterine rupture

Typically—

- Acute abdominal pain (H/O vigorous uterine contraction followed by sudden bursting pain—cessation of labour pain)
- Features of shock and intraabdoinal hemorrhage (Abdominal tanderness, guarding)
- Easily palpable fetal parts
- Absent fetal heart sound
- Contracted uterus felt on one side

Atypically

- Incomplete rupture producing localized abdominal pain and tenderness
- Frank signs of hemorrhage and rupture develop slowly

Vaginal examination:

- Bleeding through cervical os
- Recession of presenting part in complete rupture
- Cervix hangs like a curtain
- Hematuria may be present

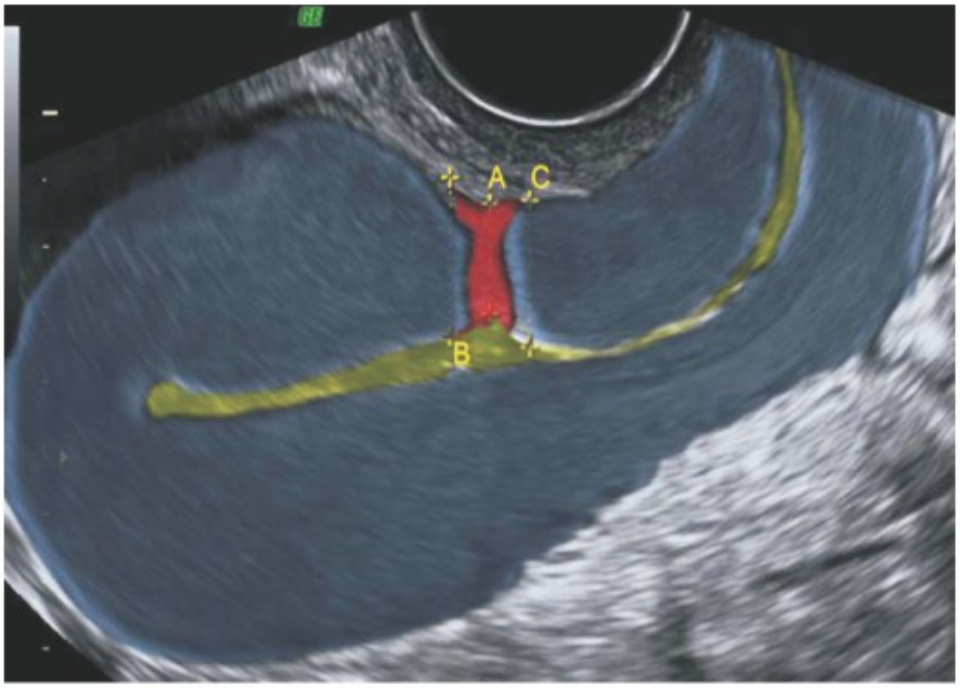
Findings on imaging

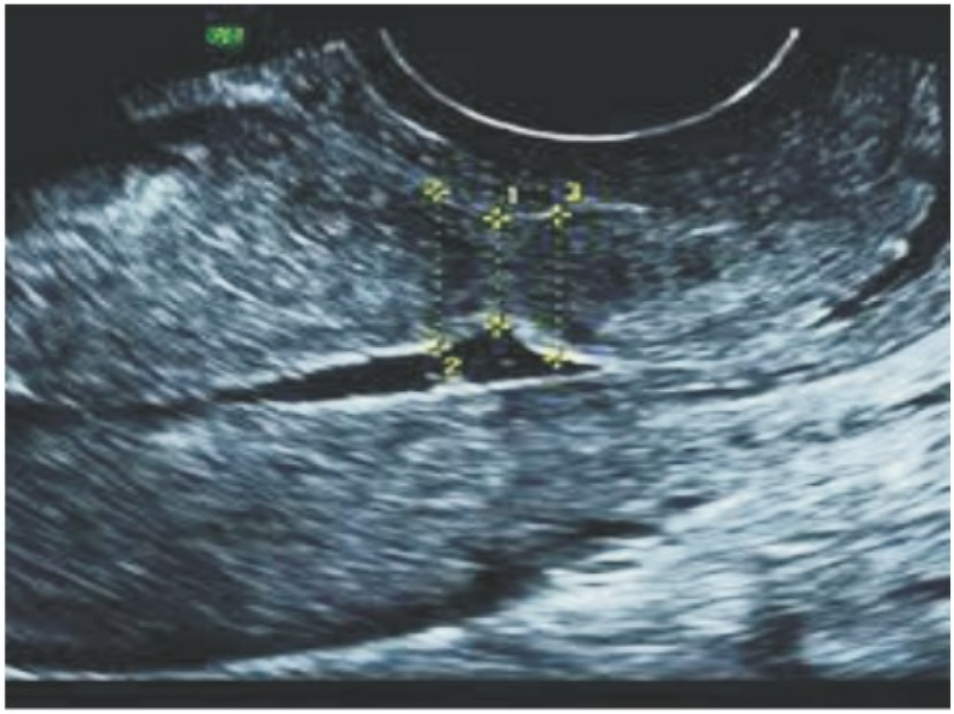
- disruption of the myometrium,
- a hematoma adjacent to the hysterotomy scar,
- extrauterine fluid-distended fetal membranes,
- free peritoneal fluid,
- an empty uterus,
- fetal parts outside of the uterus,
- and/or fetal demise.

Predicting uterine rupture

- **Antepartum imaging of the hysterotomy scar** < 2 mm predictive of an increased risk of rupture or dehiscence
- **Inter pregnancy imaging of the hysterotomy scar**

Saggital plane of the uterus obtained transvaginally 6 weeks after cesarean section (CS). (A) The thickness of the CS scar, (B) the thickness of the myometrium proximal and (C) distal to the CS scar


A
C
B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Management

- **Antepartum**
- **Stabilize patients with hemodynamic instability** –stabilized with fluids and blood transfusion, as appropriate, and prepared urgently for cesarean birth.
- **Notify the anesthesia service** –The choice of regional versus general anesthesia is based on the clinical stability of the patient and urgency of delivery.
- **Notify the neonatology service**
- **Prepare for unexpected findings at laparotomy** –
- In case of ruptured caesarean section scar, low parity, rupture wound clear cut------Repair done
- High parity, edges of rupture are ragged and irregular, anatomy distorted----Hysterectomy to be done

Management of coexistent complications

- **Atony**
- **Bladder trauma**
- **Pelvic organ injury** – Injuries to blood vessels and other pelvic organs
- **Placenta accreta spectrum** – Uterine rupture may be associated with placenta accreta spectrum

Causes of mortality

- Hemorrhage
- Shock
- Sepsis
- Mortality in intacted uterus rupture is more than scarred uterus

- Mortality is more in Classical scar than lower segment scar rupture

Statistics

- ✓ Total number of deliveries were 35973 of which 442 were cases of rupture uterus
- ✓ Majority of rupture uterus pt belong to more than 35 years
- ✓ Majority of women were grand multiparous (51.4%)
- ✓ Majority of patients with rupture uterus had scarred uterus (76.2 %)
- ✓ Cases with one caesarean section were 152 (34.4 %), two caesarean section were 78 (17.8 %) and 11 were of more than two caesarean section.
- ✓ Cases with prolong/ obstructed labour was seen in majority of rupture uterus pts.

CHAPTER-2

MATERNAL COLLAPSE IN PREGNANCY AND PUERPERIUM

Author : Dr. Radhey Shyam

Introduction

Maternal collapse is defined as an acute event involving the cardiorespiratory systems and/or central nervous system resulting in a reduced or absent conscious level (and potentially cardiac arrest and death), at any stage in pregnancy and up to 6 weeks after birth[1].

The incidence of cardiac arrest in pregnancy is much rarer than maternal collapse at around 1 : 36,000 maternalities, with a case fatality rate of 42%. Causes of maternal cardiac arrest vary including hypovolemia, thromboembolic disease, amniotic fluid embolism and cardiac causes with a significant mortality rate if occurring in the community.

An obstetric modified early warning score (MEOWS) chart along with clinical judgment should be used to allow early recognition of the woman who is becoming critically ill[1].

Causes of Maternal Collapse

General

Maternal collapse can result from many causes which may or may not be pregnancy related. If the cause is reversible, the survival rates are greater and those for which specific treatment exists must be rapidly considered [5].

Dose and duration of Infant daily NVP prophylaxis (10 mg of Nevirapine in 1ml suspension)

Infants Birth Weight (gm)	NVP daily dose (mg)	NVP daily dose (ml)	Duration
Birth weight less than 2000 gm	2 mg /kg. once daily In consultation with a pediatrician trained in HIV care	0.2 ml /kg. once daily	Up to 6 weeks* irrespective of exclusive breast feeding or exclusive replacement feeding
Birth weight between 2000 – 2500gm	10 mg. once daily	1 ml once a day	
Birth weight more than 2500 gm	15 mg. once daily	1.5 ml once a day	

*The duration of NVP to infant be minimum 6 weeks but more if ART to mother was started in late pregnancy, during or after delivery (which is less than 4 weeks), then the infant NVP should be increased to 12 weeks.

A systematic ABCDE approach should enable the clinical team to identify the most common causes of cardiac arrest.

Consider 4 'H's and 4 'T's and in the pregnant woman add eclampsia and intracranial hemorrhage.

Reversible cause	Cause in pregnancy
4 H's	
Hypovolaemia	Bleeding (obstetric/other; may be concealed) or relative hypovolemia due to dense spinal block, septic or neurogenic shock and anaphylaxis
Hypoxia	Pregnant women can become hypoxic more quickly. Cardiac events – peripartum cardiomyopathy, myocardial infarction, aortic dissection, large vessel aneurysms
Hypo/hyperkalaemia	No more likely; severe hyperemesis

Hypo/hypernatraemia	**May be caused by oxytocin use** **Iatrogenic administration of fluids in labour/ women's desire to "drink plenty of fluid" in labour**
Hypothermia	**No more likely**
4 T's	
Thromboembolism	**Amniotic fluid embolism, pulmonary embolism, air embolism, Myocardial infarction**
Toxicity	**Local anaesthetic, magnesium, other**
Tension pneumothorax	**Following trauma/suicide attempts**
Tamponade	**Following trauma/suicide attempts**
Eclampsia and pre-eclampsia	
Intracranial Haemorrhage	

Hemorrhage

Major obstetric hemorrhage was responsible for 14 maternal deaths between 2017-2019 with an estimated incidence of 6 in 1000 maternities[6]. Cause of major obstetric hemorrhage include postpartum hemorrhage, major antepartum hemorrhage from placenta praevia, placental abruption, uterine rupture and ectopic pregnancy. Concealed hemorrhage should not be forgotten including following Caesarean section and ruptured ectopic pregnancy.

In the case of massive placental abruption, Caesarean section may occasionally be indicated even if the fetus is dead to allow rapid control of the hemorrhage.

Intravenous tranexamic acid significantly reduces mortality due to postpartum hemorrhage.

Thromboembolism

Thromboembolism is the leading cause of direct maternal death during or up to 6 weeks after the end of the pregnancy leading to the deaths of 20 women in the MBRRACE report 2017-2019[6]. For full guidance refer to

Cardiac disease

The main cardiac causes of maternal death are ischaemia and sudden arrhythmic cardiac death with a structurally normal heart. Aortic root dissection, although usually associated with an inherited aortopathy can present in otherwise healthy women, and signs and symptoms, such as central chest or interscapular pain, a wide pulse pressure (mainly secondary to systolic hypertension) and a new cardiac murmur, must prompt appropriate imaging and, if required, referral to a cardiologist. The incidence of congenital and rheumatic heart disease in pregnancy is increasing, secondary to increased survival rates and with improved management of congenital heart disease. In addition, women with mechanical prosthetic heart valves are at particularly increased risk of complications in pregnancy. Other cardiac causes include: cardiomyopathy; dissection of the coronary artery; acute left ventricular failure; infective endocarditis; and pulmonary oedema.

After successful resuscitation, cardiac cases should be managed by an expert cardiology team.

Sepsis

Sepsis is a significant cause of maternal morbidity and mortality. Bacteraemia which can be present in the absence of pyrexia or a raised white cell count, can progress rapidly to severe sepsis and septic shock leading to collapse[1].

Septic shock should be managed in accordance with the Surviving Sepsis Campaign guidelines.

For full guidance refer to the 'Management of sepsis in pregnancy and puerperium guideline'.

Amniotic fluid Embolism

UK Incidence of Amniotic Fluid Embolism (AFE) reported in the 2017-2019 MBRRACE report was 0.32 per 100,000 maternities. AFE presents as a collapse during labor or birth, or within (usually) 30 minutes of birth in the form of hypotension, respiratory distress and acute hypoxia. Seizures and cardiac arrest may also occur[1]. This is followed by acute coagulopathy in those women who survive the initial event. AFE incidence is increased in women who have multiple pregnancy, polyhydramnios, placenta praevia, placental abruption and induction of labour[7]. If AFE is suspected or proved the UK National Registry for AFE should be contacted.

The management of AFE is supportive rather than specific, as there is no proven effective therapy. Coagulopathy needs early, aggressive treatment, including the use of fresh frozen plasma.

Recombinant factor VII should only be used if coagulopathy cannot be corrected by massive blood component replacement as it has been associated with poorer outcome in women with AFE

Drug toxicity and overdose

Drug toxicity and overdose should be considered in all cases of collapse. Substance misuse should be remembered as a potential cause of collapse especially outside of hospital.

Therapeutic drug toxicity is possible with commonly used drugs in obstetric practice such as magnesium sulphate in the presence of renal impairment and local anesthetic agents. The antidote to cardiac dysrhythmias, respiratory depression or resistant hypotension caused by magnesium toxicity is 10 ml 10% calcium gluconate or 10% calcium chloride given by slow intravenous injection. For further information, please refer to Toxbase®.

Signs and symptoms of Local Anesthetic Toxicity	
Mild	Severe
Tingling, numbness of the tongue or around the mouth	Sudden loss of consciousness
Metallic taste	Tonic-clonic convulsions
Mild visual disturbances	Cardiovascular collapse
Light headedness	Sinus bradycardia
	Conduction blocks
	Asystole and ventricular tachyarrhythmias

If local anesthetic toxicity is suspected, stop injecting immediately.

Lipid rescue should be used in cases of collapse secondary to local anesthetic toxicity. Intralipid 20% is available on the Resuscitation trolley.

Manage arrhythmias as usual, recognizing that they may be very refractory to treatment. All cases of lipid rescue should be reported to NHS Improvement and

the Lipid Rescue site. Refer to the Management of Local Anesthetic Toxicity in Obstetric Patients guideline.

Eclampsia

Fitting after 20 weeks gestation may be attributed to eclampsia, notably where there is no known history of epilepsy. However, epilepsy should always be considered in cases of maternal collapse associated with seizure activity.

For full guidance refer to the 'Hypertensive disorders in pregnancy guideline'.

Intracranial hemorrhage

Intracranial hemorrhage is a potential complication of uncontrolled, particularly systolic hypertension, but can also result from ruptured aneurysms and arteriovenous malformations. The initial presentation may be maternal collapse but often severe headache precedes this. Neuroradiologists and neurosurgeons should be involved in the care of pregnant women with intracranial hemorrhage at the earliest opportunity.

Anaphylaxis

Anaphylaxis is a severe, life threatening systemic hypersensitivity reaction, resulting in respiratory, cutaneous and circulatory changes, and collapse. There is significant intravascular volume redistribution, which can lead to decreased cardiac output. Acute ventricular failure and myocardial ischemia may occur.

Airway obstruction secondary to angioedema, bronchospasm and mucous plugging of smaller airways all contribute to significant hypoxia and difficulties with ventilation[1].

In cases of anaphylaxis, all potential causative agents should be removed, and the ABCDE approach to assessment and resuscitation followed.

If a cardiac arrest secondary to an anaphylactic reaction occurs in the community, the woman should have basic life support, including IM adrenalin if available, and be transferred to a hospital setting as quickly as possible, unless a suitably trained healthcare professional is present with appropriate equipment and drugs in which case definitive resuscitation and treatment should be commenced.

The treatment for anaphylaxis is 1:1000 adrenaline 500 micrograms (0.5 ml) intramuscularly. This dose is for intramuscular use only.

Physiological and anatomical changes in pregnancy that affect resuscitation.

It is essential that anyone involved in the resuscitation of pregnant women is aware of the physiological differences.

Aortocaval compression significantly reduces cardiac output from 20 weeks of gestation onwards and the efficacy of chest compressions during resuscitation.

Changes in lung function, diaphragmatic splinting and increased oxygen consumption make pregnant women become hypoxic more readily and make ventilation more difficult.

Difficult intubation is more likely in pregnancy. Weight gain in pregnancy, large breasts inhibiting the working space and laryngeal oedema can all contribute to making intubation more difficult.

Pregnant women are also at an increased risk of aspiration.

Management of the collapsed woman

Maternal collapse resuscitation should follow the Resuscitation Council (UK) 2021 guidelines using the standard ABCDE approach, with some modifications for maternal physiology, in particular relief of aortocaval compression.

In the event of maternal collapse

- Ensure safe to approach
- Stimulate and assess response

If she responds

- Call for help **Obstetric Emergency call,**

Place in **left lateral position if TILTED in theatres** or, if outside this environment, manually **and gently displace the uterus** by placing a hand below the uterus on the maternal right and pushing the uterus slightly upwards and to the **to the left** to relieve aortocaval compression.

- Give high-flow oxygen to achieve Sat O2 of at least 94%
- Commence MEOWS chart if not already in use and escalate as appropriate
- Assess fetal wellbeing.
- Check blood glucose level
- Insert 16G IV cannula
- Take bloods for:
  - ✓ full blood count
  - ✓ group and save or crossmatch 4 units dependent on

perceived cause of collapse o urea and electrolytes

- ✓ clotting studies
- ✓ Arterial blood gas/venous blood gas including lactate
- ✓ Blood cultures should be obtained by separate venous stab as per trust guidelines. All sample should be processed as URGENT by Pathology. Ongoing treatment will depend on the cause of the collapse.

If No response

- Call for **Maternal Cardiac Arrest**
- Ensure manual uterine displacement in women above 20 weeks gestation orwhere the uterus is palpable at or above the level of the umbilicus.

Airway

- Open airway
  - o Check for obstruction
  - o Head tilt, chin lift
- Assess for breathing for up to 10 seconds
  - o Look for chest movement, listen for breath sounds, feel for air
- **Breathing normally**
  - o Turn into recovery position
  - o Check help is on the way

o Assess breathing, pulse, blood pressure, fetal heart rate regularly using a MEOWS chart.

- **Not breathing, start Cardiopulmonary Resuscitation (CPR) as per Resuscitation Council (UK) 2021 guidelines**

The airway should be managed as soon as possible by an experienced anesthetist.

- Persons not directly involved with the resuscitation should ensure that: o The security doors are open to allow emergency access to the area.
  - ❖ The cardiac arrest trolley is taken to the room.
  - ❖ The consultant obstetrician and consultant obstetric anaesthetist should be summoned at the time of the cardiopulmonary arrest call.
  - ❖ Someone is available to act as a 'runner'.
  - ❖ Appoint a scribe.
  - ❖ The woman's records are available.

- Supplemental oxygen with a gas flow 10-15 liter per minute should be administered as soon as possible. Bag and mask ventilation should be undertaken until intubation

  - When the defibrillator arrives, apply self-adhesive defibrillation pads to the woman and analyze the rhythm. These should be applied whilst chest compressions are ongoing.

Circulation

- **Assess cardiac rhythm**

Shockable Rhythm	Non-Shockable
VF / pulseless VT	Asystole and PEA
Defibrilation with 200 j/300 j/360j biphasic 360 j monophasic	
CPR 30:2 for 2 minutes	Immediate CPR 30:2

- **During CPR**

Establish IO/ IV access – ideally two wide bore cannulae should be inserted as soon as possible. If peripheral venous access is not possible early consideration of intraosseous access (IO), central venous access or venous cut down should be considered. • Give adrenaline as per Advance Life support algorithm.

- **Correct reversible causes – 4 H's, 4T's**

Perimortem Caesarean Section (PMCS)

- PMCS should be seen as a resuscitative procedure to be performed primarily in the interests of maternal survival.

- Senior staff should be involved at an early stage.

- **In women over 20 weeks of gestation, if there is no response to correctly performed CPR within 4 minutes of maternal collapse or if resuscitation is continued beyond this, then PMCS should be**

undertaken to assist maternal resuscitation. Ideally, this should be achieved within 5 minutes of the collapse.

• A scalpel and umbilical cord clamps should be available on the resuscitation trolley in all areas where maternal collapse may occur, including accident and emergency.

• Perimortem caesarean section should be performed where the resuscitation is taking place.

• The operator should use the incision which will facilitate the most rapid access. This may be a midline vertical incision or a suprapubic transverse incision.

• Where the outcome is not successful, the case should be discussed with the coroner to determine whether a post-mortem is required before any medical devices such as lines and endotracheal tubes are removed, as per the Royal College of Pathologists recommendations.

What are the outcomes for the mother and the baby?

Outcomes for mothers and babies depend on the cause of collapse, gestational age and access to emergency care, with survival rates being poorer if the collapse occurs out of hospital. In maternal cardiac arrest maternal survival rates of over 50% have been reported.

Post resuscitation care

- Ongoing management depends on the underlying cause of the collapse
- It is essential the woman and baby is transferred to an appropriate environment such as high dependency or critical care area.

- Accurate documentation is essential in all cases of maternal collapse and a critical incident form (RL) should be submitted whether or not resuscitation is successful.
- All cases of maternal death must be reported to MBRRACE-UK
- All maternity staff should have annual formal multidisciplinary training in generic life support and the management of maternal collapse.
- Life support training improves resuscitation skills.
- Small group multidisciplinary interactive practical training is recommended to improve the management of maternal collapse.

CHAPTER-3

SHOCK IN OBSTETRICS

Author : Dr. Radhey Shyam

"shock during pregnancy is one of the most difficult problems faced by the obstetricians and necessitates initiation of management even before full identification of its cause for better survival"

Definition

- It is a clinical condition arising out of an inability of the circulatory system to provide adequate tissue perfusion causing cellular hypoxia and organ damage
- It is a systemic disorder affecting multiple organ systems
- Perfusion may either be decreased throughout the body or distributed poorly
- Incidence- it accounts for 0-3%

Types and causes

Hemorrhagic shock

Hemorrhagic shock due to hypovolemia is the most common cause of shock in obstetrics

- </= 1000ml compensated
- 1000-1500ml-mild
- 1500-2000ml-moderate
- >2000ml-severe

Non-hemorrhagic shock

- Septic shock due to infections
- Hypertensive disorders
- Anesthesia
- Cardiogenic
- Neurogenic
- embolism

Causes

➢Commonest of all is atonic PPH

❑ Early pregnancy

- Abortion
- Ectopic pregnancy
- Gestational trophoblastic disease

❑ Antepartum hemorrhage

• Placenta previa

- Abruptio placenta
- Rupture uterus

❑ Post-partum hemorrhage

- Traumatic PPH
- Atonic PPH

Clinical Features

- Pallor
- Rapid and thready pulse
- Low blood pressure
- Cold clammy extremities
- Air hunger
- Diminution of vision
- Oliguria
- Anuria

Phases of Hemorrhagic shock

Phase of compensation

- Blood loss less than 15%
- Postural hypotension is noted
- Sympathetic stimulation is the initial response leading to peripheral vasoconstriction to maintain blood supply to vital organs
- ↓ venous return causes ↓CO due to constriction of pre and post capillary sphincters

Clinical picture

- Pallor
- Tachycardia
- Normal blood pressure
- Tachypnea
- Sweating
- Hyperventilation
- At this phase, transfusion resuscitation and control of hemorrhage are

usually effective in restoring the normal circulation and perfusion

Phase of Decompensation

- Blood loss is 20-35%
- Blood loss exceeds 1000ml in normal patient or less if other adverse factors are operating like severe anemia.
- There is relaxation of precapillary sphincters and damage to the microcirculatory bed due to thromboxane A2 and leukotrienes.

Clinical picture

- Classic clinical picture of shock
- Cold and clammy skin
- Tachycardia
- Tachypnea
- Low pulse pressure
- Low systolic pressure
- Adequate treatment at this phase improves
- If untreated it can become irreversible by passing onto the phase of cellular damage
- Venular walls mediators d/t tissue damage
- Progressive vasodilatation vascular permeability
- Peripheral pooling of blood

Clinically at this stage the patient has features of coma, worsened heart function and progressive renal failure due to acute tubular necrosis

Hypovolemic shock

"speed is vital and rapid restoration of the circulating blood volume is the key to successful outcome"

- Establishment of airway and oxygen therapy at a rate of 6-8 L per minute

to maintain O2 saturation of > 92% and PaO2 of 80 100 mm Hg

- ET intubation and mechanical ventilation are required for severe hypoxia, severe tachypnea and coma to maintain oxygen supply
- Establishment of two wide bore IV lines
- Elevation of legs to facilitate venous return
- Keep the women warm
- Plasma expanders, like, hemaccel may also improve the microcirculation
- They will remain in circulation for 24hrs to 48hoursrs
- Plasma protein fraction or fresh frozen plasma and later, when available, whole blood preferably packed cells should be transfused quickly
- Insert a foleys catheter to measure urine output
- Positioning of the patient in the trendelenburg tilt may aid the venous return

Drug therapy

- Analgesics- 10-15 ml morphine intravenously if, there is pain, tissue damage or irritability
- Corticosteroids- hydrocortisone 1g or dexamethasone 20 mg slowly (IV), It may reduce the peripheral resistance and potentiate cardiac response to improve tissue perfusion
- Sodium bicarbonate 100 mEq IV, if metabolic acidosis is demonstrated
- Vasopressors to increase the blood pressure so as to maintain renal perfusion
  a) Dopamine 2.5-10 micrograms/kg/min by IV infusion is the drug of choice
  b) Beta adrenergic stimulant isoprenaline 1mg in 500ml 5% glucose slowly IV infusion

c) Digitalization may be carried out if inspite of volume replacement the CVP remains high due to myocardial failure. This is unlikely unless as a terminal event

d) Vasodilators – phenoxybenzamine an alpha receptor blocker is given as 1mg/kg over 1 hr IV if it is felt that the vasoconstriction is persisting inspite of adequate volume replacement

- As this management is being done, simultaneously ultrasound examination is carried out to find the cause of blood loss and assess the fetus in antenatal patients and to rule out placental bits in postpartum patients
- In addition to medical management, surgical intervention depending upon the cause of hemorrhage like emergency cesarean for antepartum hemorrhage, laparotomy, internal iliac ligation or hysterectomy for severe postpartum hemorrhage may be required
- Volume replacement should initially be done by crystalloid solutions

Monitoring is done by-

- Assessment of central venous pressure
- Pulse rate
- Blood pressure
- Urine output
- Pulmonary capillary wedge pressure
- By clinical improvement in
- pallor
- Cyanosis
- Air hunger
- Sweating

Non Haemorrhagic Shock Septic shock

- It refers to sepsis- related hypotension that persists in spite of adequate fluid replacement
- Incidence 1 in 8000
- Maternal mortality can reach 13% in severe sepsis and up to 30% in septic shock.
- Neonatal mortality can be as high as 40%

Predisposing factors

Septicemia and septic shock usually occur following maternal infection at one of the following sites:

- pyelonephritis due to anatomic alterations in the renal tract in pregnancy
- Endometritis in the puerperium due to large area of denuded maternal tissues exposed to bacteria
- Septic abortion where inadequate evacuation of the products provides a nidus for bacterial proliferation
- Perforation of uterus with peritonitis
- Infection of surgical wounds, where a breach in the skin is liable for bacterial contamination

Clinical criteria for diagnosis of sepsis

- Infection and bacteremia may lead to sepsis, which is diagnosed by the presence of the following signs:
  - Fever or hypothermia
  - Tachycardia
  - Tachypnea
  - Leukocytosis or leukopenia
  - Thrombocytopenia

- Hypoxemia
- Oliguria
- Increased serum creatinine

As the sepsis worsens, severe sepsis is diagnosed by the appearance of the following signs:

- Hypotension
- Worsening oliguria- urine output 30ml/hr for 2 hrs
- Worsening renal failure- serum creatinine > 2mg/dl
- Acute lung injury
- Serum bilirubin >2mg/dl
- Platelets<1000000 mm3
- Prothrombin time >1.5

Lysis of gram –ve bacteria

↓

Endotoxin (LPS) in circulation + LPS protien

↓

CD14 molecule on surface of monocyte/ macrophage elaborates proinflammatory Cytokines TNF α & IL-1

↓

Promote vascular injury Vasodilatation & hypotension

Activationof inflammatory responses

- C5a and C3a → microemboli and endothelial damage
- mast cells → histamine release and increased capillary permeability
- Coagulation system→enhances development of thrombi
- Kinin system→releases bradykinin, causes vasodilation and increased vascular permeability

- ❖ The net result of above mechanisms is vasodilatation and increased vascular permeability in septic shock
- ❖ Profound peripheral vasodilatation and pooling of blood causes hyperdynamic circulation in septic shock, incontrast to hypovolemic shock
- ❖ Increased vascular permeability causes development of inflammatory oedema
- ❖ DIC is prone to develop in septic shock due to endothelial cell injury by toxins
- ❖ Reduced blood flow produces hypotension, inadequate perfusion of cells and tissues

Causative organisms and toxins

Causative organisms

- o E.coli, klebsiella, pseudomonas cause pyelonephritis and endo metritis (ENDOTOXIN)
- o Anaerobes and above mentioned bacteria causes pelvic infection and septic abortion (ENDOTOXIN)
- o Group A hemolytic streptococci staph aureus methicillin resistant staph auerius Clostridium perfringens Causes wound infection

Toxins

- Toxic shock syndrome like toxin
- TSST 1
- Super antigen exotoxin

Clinical features of septic shock

- ✓ Abrupt onset of fever, chills, and tachycardia

It has the following phases

- ✓ Warm phase- phase of peripheral vasodilatation Tachycardia, Hypotension, Warm extremities, Low CVP due to marked decrease in intravascular fluid volume
- ✓ Cold phase- phase of peripheral vasoconstriction Elevated CVP due to cardiac failure, Poor tissue perfusion and lactic acidosis, Tachypnea, Adult respiratory distress syndrome, Altered sensorium, DIC
- ✓ Multiorgan failure due to hypotension and DIC
- ✓ Acute renal failure, Altered LFT, Respiratory failure, Cardiac failure

Diagnosis of septic shock

History

- ☐ Risk factors-
  - Septic abortion
  - Puerperal endometriosis
  - Pyelonephritis
  - Wound infection
- ☐ **Symptoms and signs**
  - Fever, chills
  - Hypotension
  - Tachycardia, Tachypnea

Evidence of multi organ failure

Oliguria/anuria, Respiratory distress, DIC, Cardiac failure, Altered sensorium

Management

- When sepsis is suspected, a three- pronged strategy is instituted
- All the steps are undertaken concurrently to
- Initiate emergency goal-directed treatment
- Identify the organism and antibiotic therapy
- Find the source of infection

Emergency goal directed treatment

- Achieve hemodynamic stability
- The women should be admitted to ICU
- IV access should be established through a central vein
- The bladder is catheterized and urine sent for culture
- Rapid infusion of IV NS 2-4 L to get the CVP upto 8-12 cm and maintaining a urine output of 30-50ml/hr is mandatory
- O2 administration through venturi mask to achieve a saturation of >95% and PaO2 of >65%. If this is unsuccessful, the patient may need to be intubated and ventilated
- Patients in whom hypotension persists even after rapid IV fluid administration, press or agents like dopamine, norepinephrine, dobutamine may have to be considered

Identification of organisms and antibiotic therapy

Blood, urine, and pus are sent for culture

Pending culture reports, , antibiotics are started

- Initial therapy
  - Ampicillin or augment in and gentamicin, Meropenam and aztreonam for gram- negative infections
- Additional therapy- surgical wound infections
  - Cloxacillin - suspected staphylococcal infection
  - Vancomycin/linezolid-suspected MRSA
  - High dose benzyl penicillin 20,00,000 units 24hrly –suspected group A beta hemolytic streptococci
  - Clindamycin- necrotizing fasciitis
  - High dose benzyl penicillin and clindamycin/ metronidazole suspected clostridial myositis

Identification of site of infection

- Unless the site of infection is identified and the pus or infected tissue removed, it is not possible to eradicate the infection.
- Site of infection is identified by clinical examination, ultrasonography, computerized tomography, and/ magnetic resonance imaging when required
- If the uterus is found to be gangrenous, an emergency hysterectomy may be lifesaving.
- Pelvic abscess should be drained by colostomy.
- Laparotomy is indicated when there is intraabdominal collection of pus

Neurogenic shock

May be due to painful conditions like

- Acute inversion
- Rapid evacuation of uterine contents
- Vasovagal stimulation

- Spinal anesthesia may cause serious hypotension due to blockade of the normal sympathetic vasomotor tone Management
- General measures like fluid replacement
- Correction of acidosis
- Vasoactive drugs
- Corticosteroids
- Ventilation and elimination of the source of neurogenic stimulus

Acute inversion

- Acute inversion after delivery can be the cause of neurogenic shock
- Causes-MC mismanaged 3rd stage of labor seen outside the vulva

Management

- Immediate resuscitation must be started simultaneously with the efforts to reduce inversion
- Intravenous fluids must be infused with a wide bore cannula pending the arrival of cross-matched blood for transfusion.
- Ergometrine or oxytocin should not be given, as these will only aggravate matters and make reduction or replacement of the uterus more difficult
- Inversion should be immediately replaced without attempting to remove the placenta from the inverted fundus, which can be delivered later

Amniotic fluid embolism

It is a rare obstetric emergency in which amniotic fluid, fetal cells, hair or other debris enter the maternal circulation, causing cardiorespiratory collapse Risk factors

- Older maternal age

- Induction of labor using prostaglandins instead of oxytocin
- Multiple pregnancy
- Polyhydramnios
- Placenta previa
- Placental abruption
- Operative deliveries
- Eclampsia
- Cervical lacerations and uterine rupture

Diagnosis

- Sudden onset of cardiorespiratory arrest, or both hypotension i.e. systolic blood pressure <90 mmHg and respiratory compromise
- DIC after appearance of the initial signs or symptoms. Coagulopathy must be detected before loss of sufficient blood to itself account for delusional or shock-related consumptive coagulopathy
- Clinical onset during labor or within 30mins of delivery of placenta
- No fever during labor

Management

- Patient should be admitted to ICU
- Management is supportive as there is no specific therapy for AFE
- Immediate administration of O2 and IV fluids are most important measures to prevent further hypoxia and restore circulation
- If hypotension does not respond to fluids alone, vasopressors like dopamine or norepinephrine should be infused
- Deranged coagulation parameters should be treated by, cryoprecipitate or fibrinogen FFPs
- Plasmapheresis and hemofiltration have been shown to be successful in arresting the progress of the disease , probably by clearing the plasma of cytokines

Pulmonary thromboembolism

- It occurs due to thrombus blocking pulmonary artery
- The symptoms depend on size of the artery obstructed and there by the area of the lung which is not perfused
- Women are at higher risk of venous thromboembolic disease in pregnancy due to the physiological changes in pregnancy which promote venous stasis and hypercoagulability of blood
- .The risk increases further during the postpartum period due to endothelial injury that occurs during delivery

Signs and symptoms

- Sudden onset dyspnea
- Chest pain
- Features of collapse like tachycardia, cold clammy skin and syncope
- Chest pain may occur anywhere in the chest and may radiate to the shoulder, arm or jaw
- It is often associated with cough and hemoptysis

Diagnosis and Treatment

- The diagnosis is easier in women with clinical suspicion of deep vein thrombosis like redness, swelling and tenderness over a vein in one of the legs
- Women with previous history of DVT should have a thrombophilia screen, preferably before pregnancy, because of the effect of pregnancy
- Low molecular weight heparin is as effective as unfractionated heparin for the acute treatment of pulmonary embolism
- Anti-coagulation must be continued for 3-6 months with either LMWH,

or alternatively warfarin, which can be started once the acute phase is over

- Warfarin is not contraindicated during lactation

Air embolism

- For an air embolus to enter the circulation, atleast part of the placental site must be exposed
- Risk factors
  - Trendelenburg position
  - Abruptio placentae
  - Placenta previa
  - Exteriorization of the uterus
  - Manual extraction of placenta
  - Severe preeclampsia
  - APH
  - Hypovolemia

Symptoms and diagnosis

- A lethal embolism may follow a bolus of 3 -5ml of air
- Tachypnoea
- Chest pain
- Gasping
- The diagnosis may be facilitated by pre-cordial doppler monitoring, transoesophageal echocardiography

Management

- Unfortunately, there is seldom time for effective treatment
- A useful immediate first aid procedure is to place the patient in the head

down, lateral position in the hope of displacing the bolus of air towards the apex of the right ventricle

- Management includes aspiration of air, discontinuation of nitrous oxide, administration of 100% oxygen and flooding the surgical site with saline to avoid further air entry

Rupture uterus

- It is a condition that carries a very high mortality, if neglected through failure to diagnose it
- The diagnosis is not easy, particularly in incomplete rupture, but if shock persists inspite of adeqauate blood transfusion to replace bloodloss, this possibility should be excluded DIC

DEFINITION

Activation of coagulation in the microcirculation by entry of large amounts of tissue thromboplastin or widespread endothelial injury leading to activation of the intrinsic pathway of coagulation and consumption of coagulation factors with a resultant bleeding diathesis

Changes in normal pregnancy

- Pregnancy is considered to be a compensated hypercoagulable state due to the changes that occur in the coagulation pathways
- Platelet count marginally decreases, but platelet aggregation increases
- There is an increase in fibrinogen and factors 7,8,9,10
- Thrombin activation is enhanced
- The fibrinolytic pathway as represented by plasmin activity is partly suppressed

Causes of DIC in pregnancy

- Placental abruption- large amounts of thromboplastin at the sites of abruption
- Amniotic fluid embolism- fetal squares, fetal antigens, anaphylactic reaction
- Sepsis syndrome- endotoxins, exotoxins, SIRS, cytokine storm, endothelial injury
- Eclampsia and HELLP syndrome- endothelial injury
- IUFD- release of thromboplastin from placenta
- Acute fatty liver of pregnancy- endothelial injury, decreased production of coagulation factors from liver

Clinical features

- Bleeding from venepuncture sites
- Ecchymoses
- Oozing/bleeding from incisions/lacerations/placental site
    1) . Episiotomy
    2) Cesarean section incisions
    3) . Profuse vaginal bleeding
- Hypotension and shock

Symptoms due to clotting in microvasculature

1) Tissue hypoxia and lactic acidosis
2) Decreased urine output
3) Metabolic acidosis
4) Acidotic breathing

5) Hypoxia and tachypnea, altered sensorium

Diagnosis

- A H/O predisposing obstetric events such as abruption, sepsis, or amniotic fluid embolism is usually present
- Clinical features of bleeding, ecchymosis, or end-organ failure are sufficient to make a clinical diagnosis
- Whole blood clotting time is markedly prolonged, a bedside clot retraction test can be performed by collecting a blood sample in a plain tube and observing the time taken for formation of clot, in established DIC, clot may not be formed for several hours and even if a clot is formed, it is soft and friable and does not retract
- All bleeding parameters such as bleeding time, clotting time, prothrombin time, partial thromboplastin time, and thrombin time are prolonged
- Peripheral smear shows thrombocytopenia and schistocytes
- Plasma fibrinogen is markedly decreased. High levels of fibrinogen and fibrin split products are present in the peripheral blood, these products inturn inhibit formation of fibrin and cause a vicious cycle

Management

- Control of hemorrhage, replacement of blood and blood products, and treatment of the underlying cause
- Packed cells are used for correction of anemia
- Platelet concentrates for treating thrombocytopenia
- Fresh frozen plasma or cryoprecipitate to replenish deficient factors
- Recombinant factor 7a can be used in uncontrollable bleeding, but its use may be associated with increased risk of stroke or pulmonary embolism

➢ Concurrently the underlying obstetric condition should be promptly managed.

Cardiogenic shock

- Circulatory collapse caused by failure of the heart to pump blood adequately

Etiology

Failure of left ventricular ejection due to

- Cardiac arrest
- Myocardial infarction
- Failure of ventricular filling
- Cardiac tamponade
- Pulmonary embolism
- Any cause of obstetric shock can result in cardiac arrest

Cardiac arrest

✓ A variety of conditions, pregnancy related and non pregnancy related can cause cardiac arrest

✓ Most frequent reasons for cardiac arrest in pregnancy and postpartum are obstetric hemorrhage (38.1%) followed by AFE(13.3%), acute coronary syndrome (10%) and venous thromboembolism in 4%

- Anesthesia
- Bleeding
- Cardiovascular disorders
- Drugs
- Embolism
- Sepsis

- General causes like metabolic and electrolyte imbalance
- Hypertensive disorders including stroke

Management

- ❖ It is same as in non-pregnant woman
- ❖ Epinephrine is vasopressor of choice and should be administered by intravenous or intraosseous access above the diaphragm
- ❖ Prompt resuscitation of the mother provided on the spot can save both maternal and fetal life
- ❖ However resuscitation is difficult in pregnant patients due to the physiological changes of pregnancy

Physiological changes in pregnancy and cardiopulmonary resuscitation

- ☐ The implication of these hemodynamic changes in a bleeding pregnant patient may lose up to 30-35% of her blood volume before manifesting signs like tachycardia and hypotension, although the fetal circulation suffers severely due to this loss
- ☐ An abnormal fetal heart pattern may be the first sign of significant maternal blood loss
- ☐ oxygen demand of the pregnant mother increases and the functional residual capacity of the lungs decreases due to elevation and splinting of the diaphragm by the enlarging uterus, intubation and ventilation may be difficult in obese women.
- ☐ Gastroesophageal sphincter is less competent due to the hormonal effects of the pregnancy which increase the risk of regurgitation of gastric contents and aspiration pneumonitis, H2 receptor antagonists can be given to reduce gastric acidity
- ☐ Patient should be placed in left lateral position to releive aortocaval compression.

Basic life support

Must be instituted immediately while preparations are being made to gain an intravenous access to correct hypovelemia

- ☐ Airway and breathing
- **Head tilt, chin lift manouver after ruling out head and neck injuries, jaw thrust manouver in case of head and neck trauma are recommended to open the airway Suction can be used to clear the airway**
- **100% oxygen should be provided by a reservoir bag**
- **Carotid pressure should be maintained to prevent gastric contents regurgitation**
- ☐ Circulation-
- Chest compressions are given by applying rhythmic pressure over the sternum, which initiates circulation by increasing the intrathoracic pressure and directly stimulates the heart
- Patient should be placed in supine position with the uterus displaced manually to left side if patient is >20 weeks POG in order to prevent aortocaval compression

Advanced life support

- ➢ Inhalation – with a cuffed endotracheal tube
- ➢ Vasopressor- epinephrine should be administered to patients with cardiac arrest in a dose of 1mg every 3-5 mins during CPR

Defibrillation

Mendelson syndrome

- Gastric contents that are highly irritant may be inhaled during induction of anasthesia
- Chemical pnemonitis is more likely following aspiration of gastric contents
- Factors that increase risk
  - Emergency surgical procedures
  - Inadequate depth of anaethesia
  - Obesity
  - Concomittant opioid administration
  - Impaired concsiousness
  - Lithotomy position
  - Difficult airway or intubation
  - Gastro intestinal reflux ,Hiatal hernia

Clinical features and prevention

- ☐ May appear between 2-5 hrs after anaesthesia
- ☐ Cyanosis
- ☐ Tachycardia
- ☐ Dyspnea
- ☐ Wheeze
- ☐ Crepitant rales
- ☐ Decreased arterial oxygen tension

Prevention

- ➢ Solid foods should be avoided in labouring patients and those at additional risk factors including diabetes, morbid obesity and a difficult airway
- ➢ Antacids decrease the risk of aspiration by increasing the pH of gastric contents

Treatment

- Patient should be placed in Trendelenburg position and oropharynx suctioned
- If signs of hypoxia present- patient should be intubated
- Bronchoscopy or pulmonary lavage should be done to remove particulate matter from the lungs
- Mechanical ventilation may be required depending on the patients condition

CHAPTER-4

ROLE OF OBSTETRICS ULTRASOUND IN HIGH RISK PREGNANCY

Author : Dr. Saurabh Kumar

ROLE OF UTERINE ARTERY DOPPLER IN HIGH RISK PREGNANCY

High risk pregnancy?

Any pregnancy that carries increased health risks for the mother, fetus or both

MEDICAL RISK FACTORS FOR A HIGH-RISK PREGNANCY?

- Chronic illness (DM, HTN, autoimmune disease)
- Low body weight (BMI of less than 18.5).
- Obesity
- Blood clotting disorders.
- BOH
- Multiple gestation (pregnancy with more than one fetus, such as twins or triplets).
- Preeclampsia and eclampsia.
- Previous preterm labor or birth, or other complications with previous pregnancies.

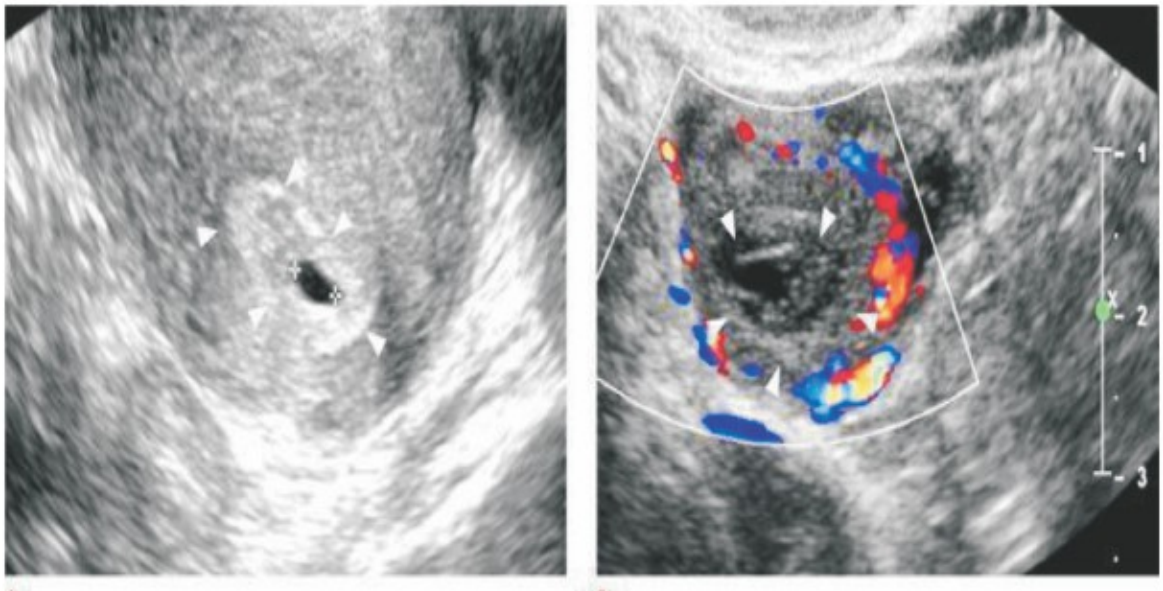
COMPLICATIONS OF HIGH-RISK PREGNANCY

- Preterm delivery.
- APH/ PPH
- Low or high birth weight baby.
- Birth defects.
- Recurrent neonatal infections ¯⊓
- Miscarriage.
- Stillbirth

FIRST TRIMESTER USG

- <3 weeks POG following conception is biggest limitation for GS.
- Normal growth rate of the GS ~1.1 mm/day.

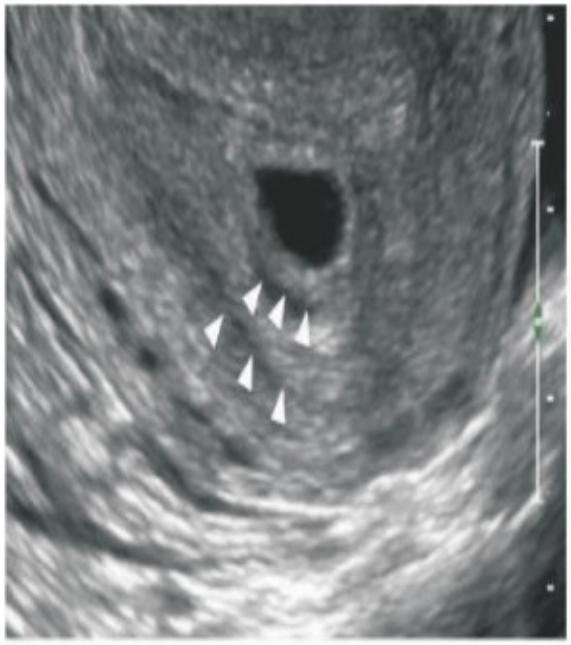
GS first becomes apparent on TVUS at approximately 4.5-5 weeks of gestational age.



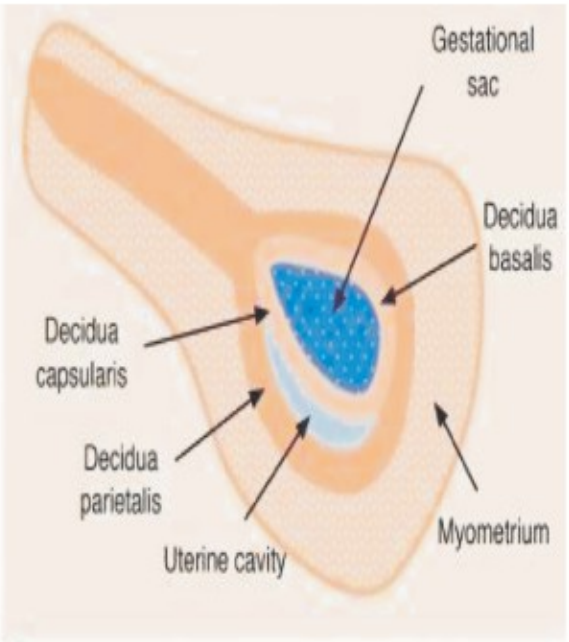
Normal early gestational sac(A) and corpus luteum(B)

DOUBLE DECIDUAL SAC SIGN

- A definitive sign of an intrauterine pregnancy (IUP).
- *While the presence of the DDS sign confirms an iup, its absence does not exclude an IUP.*
- Outer bright ring represents the decidua parietalis, while the inner ring represents the decidua capsular is and chorion.
- GS is measured in 3 dimensions and the mean sac diameter (MSD) should be calculated.



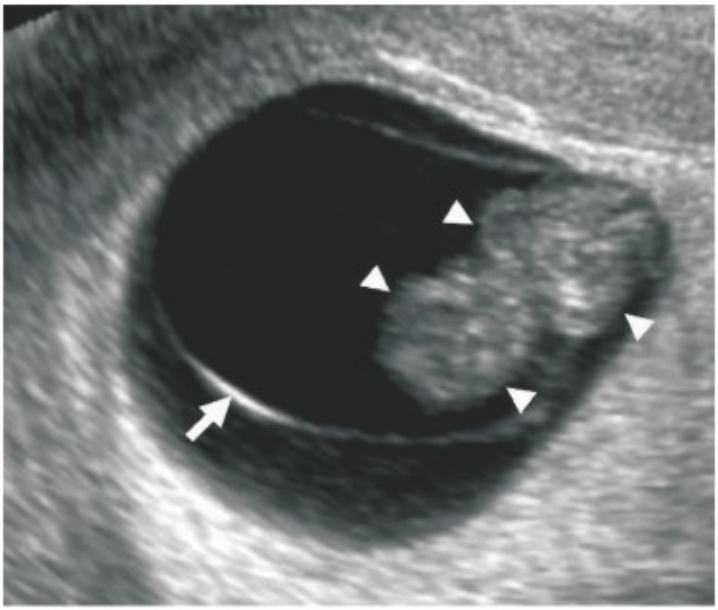
A



B

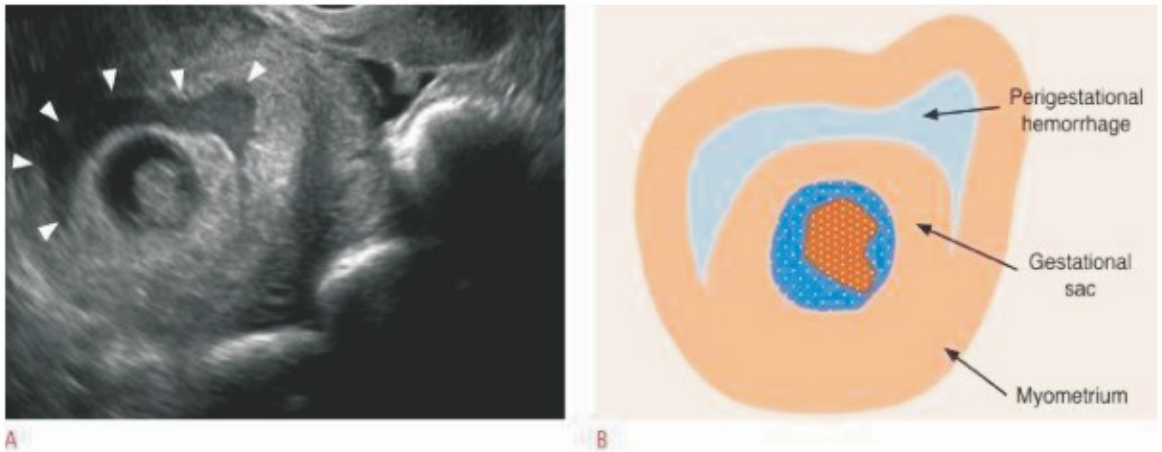
AMNIOTIC MEMBRANE

- The amniotic membrane becomes visible around 7 weeks.
- CRL closely corresponds to the amniotic sac diameter between 6.5 and 10 weeks of gestation



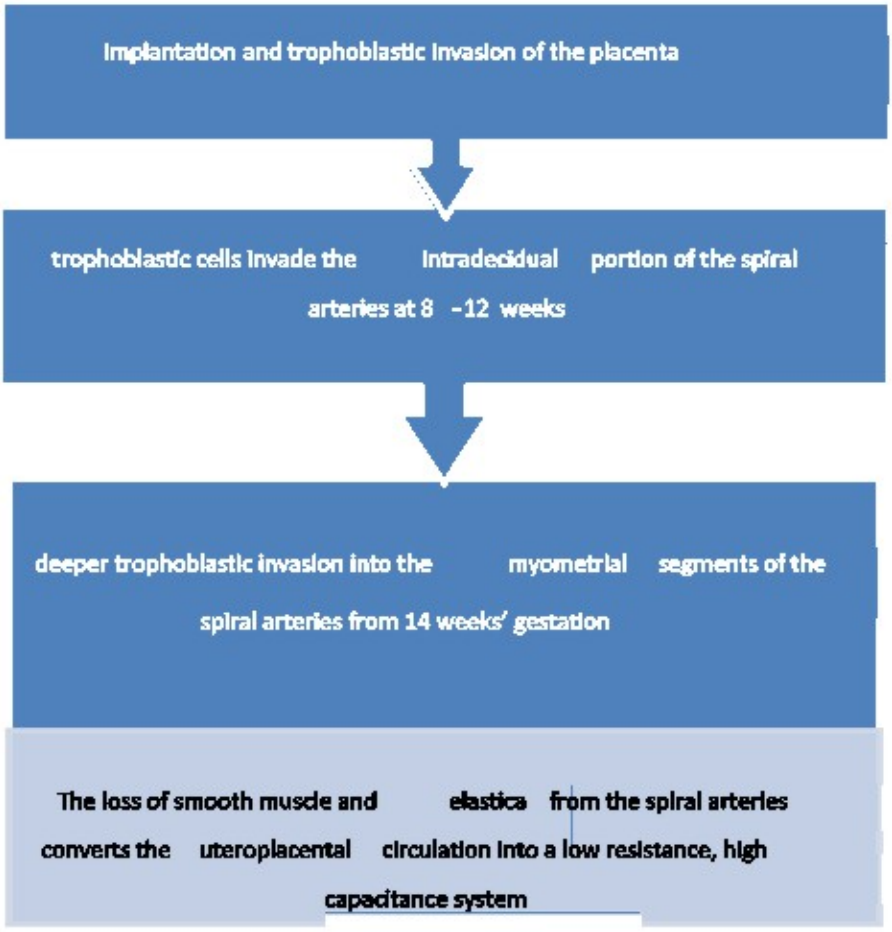
SUBCHORIOIC HEMATOMA

- occur in 18%-22% of IUPs.
- On TVUS, SCH appears as a crescent-shaped, heterogeneous avascular collection between the gestation.
- Larger sub chorionic hematomas are associated with an increased risk of pregnancy loss, especially if the hematoma is greater than 2/3rd of the chorionic circumferential sac and decidua basalis.



Sub chorionic hemorrhage.

PLACENTAL DEVELOPMENT



FIRST-TRIMESTER UTERINE ARTERY DOPPLER ANALYSIS IN THE PREDICTION OF LATER PREGNANCY COMPLICATIONS

First-trimester doppler interrogation of the uterine artery performs better in the prediction of early-onset than late-onset preeclampsia.

UTERINE ARTERY DOPPLER

- An abnormal uterine artery PI in the first trimester was predictive of preeclampsia and early-onset preeclampsia with sensitivities of 26.4% and 47.8%, respectively.

- First UA doppler to be done between 11 and 14 weeks gestation in high risk pregnancy.
- The Doppler assessment was repeated during the 22–24 week scan and again between 28 and 32 weeks gestation.
- The presence of UA notching and a PI > 1.5 during the first trimester were considered indicative of increased vascular resistance in the placental bed.

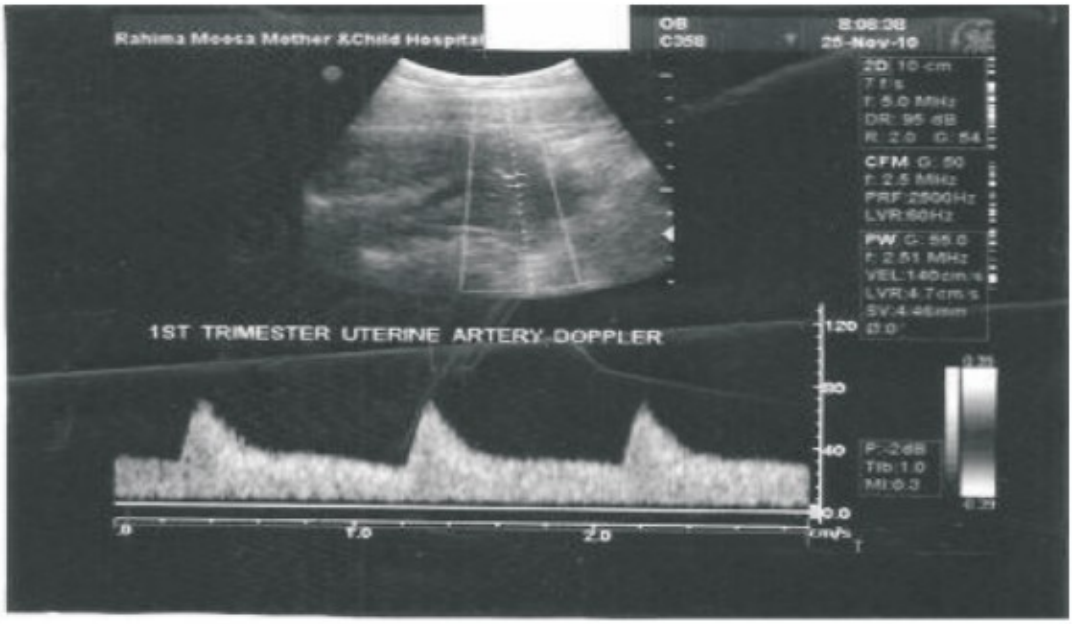
ULTRASOUND CRITERIA FOR DEMONSTRATION OF HIGH RESISTANCE FLOW WERE GUIDED BY

Table 1 – Profile of patients who developed pre-eclampsia.

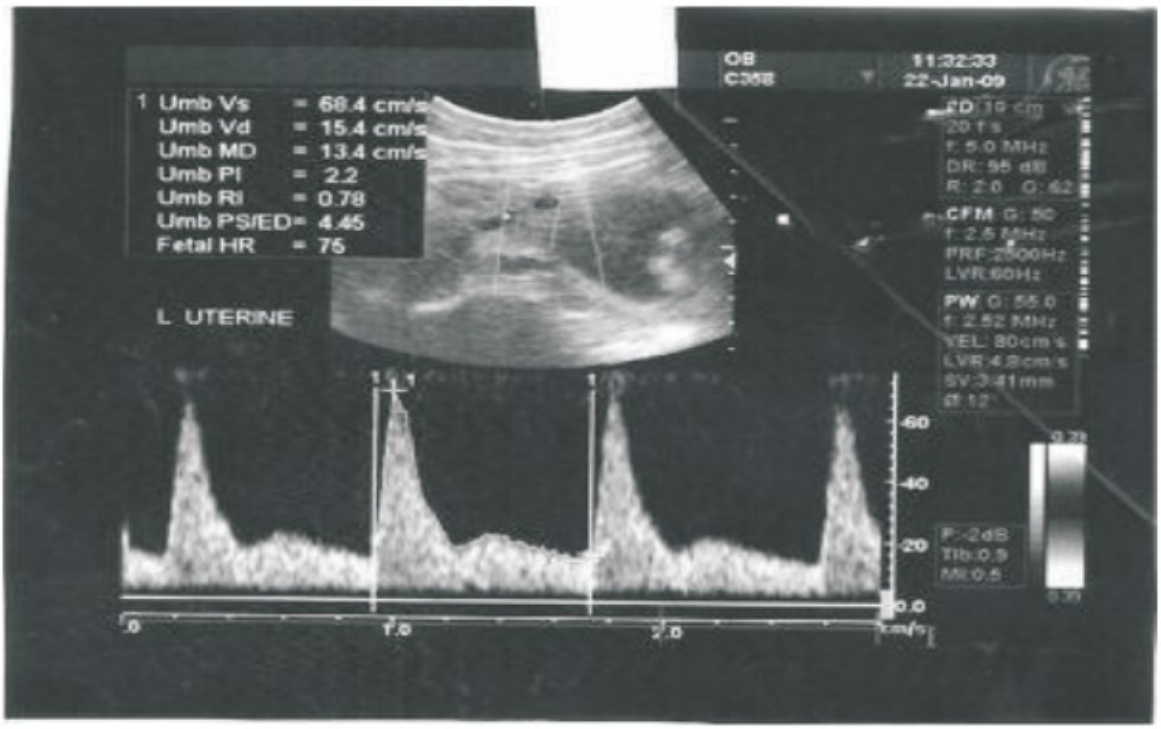
Patient number	Patient profile	Predisposing factors	Pulsatility index per trimester			Presence/Absence of notching per trimester			(
			1st	2nd	3rd	1st	2nd	3rd	
5th centile			1.1	0.7	0.6				
50th centile			1.7	1.0	0.8				
95th centile			2.7	1.5	1.2				

UTERINE ARTERY NOTCHING

- The presence of notching in the second trimester has been associated with a high probability for developing preeclampsia.



Normal 1st trimester uterine artery Doppler waveform



Abnormal uterine artery Doppler waveform with notching and a high PI in the 1st trimester

IMPLICATIONS OF UA DOPPLER FOR PRACTICE

UA Doppler screening is beneficial to patients at high risk for developing PET so that preventative therapies can be initiated early in pregnancy.

GUIDELINES FOR SCREENING HIGH RISK PREGNANCY

THE FOLLOWING ULTRASOUND GUIDELINES ARE RECOMMENDED WHEN SCREENING FOR PET

FIRST TRIMESTER SCREENING

Determine the gestational age for monitoring of fetal growth.

UA Doppler assessment: Patients with PI values > 1.5 and uterine notching only require BP monitoring on a two-weekly basis.

SECOND TRIMESTER FOLLOW-UP

- Routine fetal anatomy scan at 22 weeks gestation.
- Liquor volume assessment for signs of oligohydramnios.
- Biometric fetal growth monitoring.
- UA Doppler assessment: Patients with PI values < 1.0 (50th centile) and/or absent notching do not need a follow-up third trimester scan. 5. Patients who screen positive for PET, with ultrasound or clinically, should be followed up in the third trimester at 28 weeks.

THIRD TRIMESTER FOLLOW-UP

1. Biometric growth monitoring for signs of fetal growth restriction (FGR).

2. Liquor volume assessment for signs of oligohydramnios.
3. UA Doppler assessment. Patients with:
    a) clinical signs of PET and/or
    b) PI values of > 0.8 (50th centile) and/or
    c) UA notching and/or
    d) ultrasound features in keeping with FGR


राज्य स्वास्थ्य एवं परिवार कल्याण संस्थान, उ0प्र0
SIHFWUP
उत्तर प्रदेश सरकार
ज्ञानावृते न मुक्तिः

CHAPTER-5

PRENATAL GENETIC TESTING

Author : Prof. Rekha Sachan

Introduction

- Enables early diagnosis of congenital abnormalities, aneuploidies, and other genetic syndromes in foetus, before birth.
- The population risk of having congenital abnormality is 3% to 5%.

Aims of prenatal counselling and diagnosis

- understand and acknowledge the indications.
- understanding the medical aspects of genetic disorder
- make informed choices and describing potential diagnostic methods.

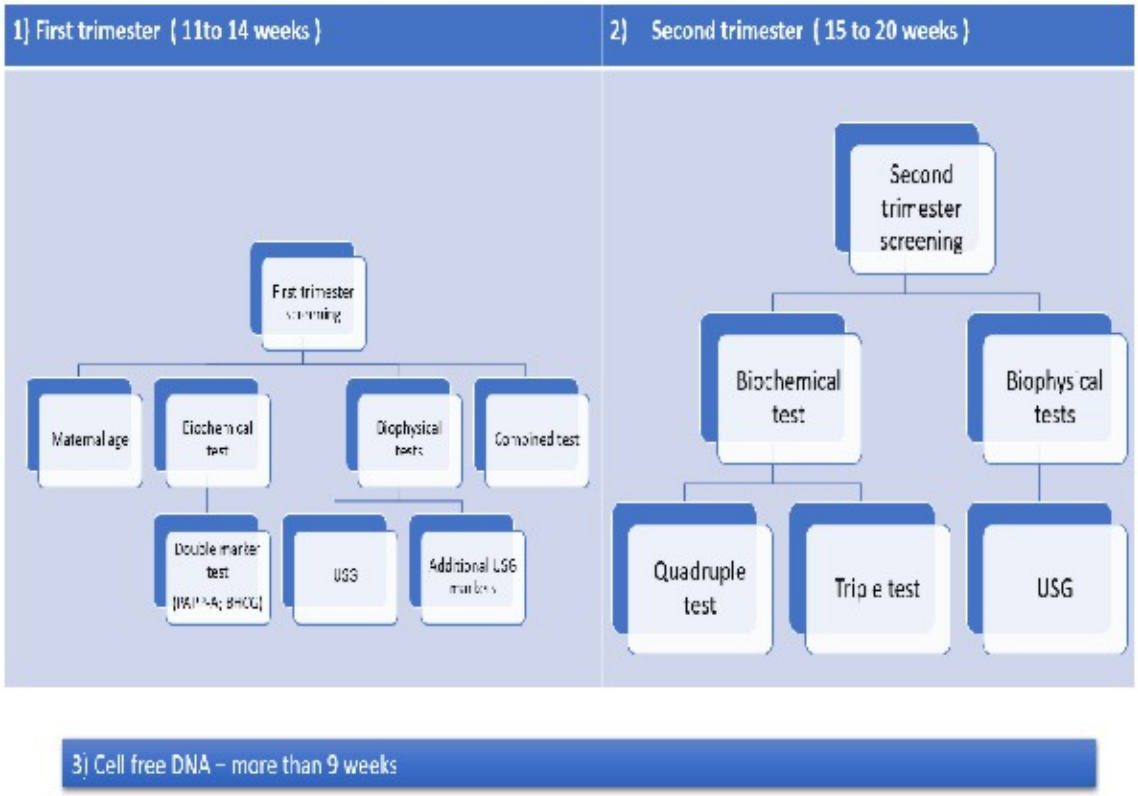
informed consent

- Made solely by women / couple concerned
- All risks, advantage and disadvantage of prenatal test to be explained.

Types of prenatal genetic tests

1-**Prenatal *screening tests*:**

(if positive indicates chances that fetus has an aneuploidy and a few additional disorders)



2-Prenatal *diagnostic tests:*

(if positive indicates fetus actually has an aneuploidy or specific inherited disorders)

Factors requiring first trimester screening

***1)* Maternal age**

Advanced age increases the chances of having a pregnancy affected by a chromosomal abnormality.

Risks of Trisomy 21, 13, 18 increases with advancing age

But the risk decreases with advancing gestational age.

2) Double marker

Tests	Double marker
Components	Human chorionic gonadotropin, Pregnancy associated plasma protein (Both produced by placenta)
Gestational age	11 and 14 week
Sample	Maternal blood
Detection rate	Performing PAPPA at 9wk and beta HCG at 12 wk increase the sensitivity of screening for downs to 95 %
Trisomy 21	Hcg ↑ PAPP-A ↓
Trisomy 18 and 13	Hcg ↓ PAPP-A ↓

Measurement

- **Mom (multiples of median) measure how far individual test result deviates from median**
- **MoM = Result (patient)/median (patient population).**

Analyte based screening test is based on composite likelihood ratio

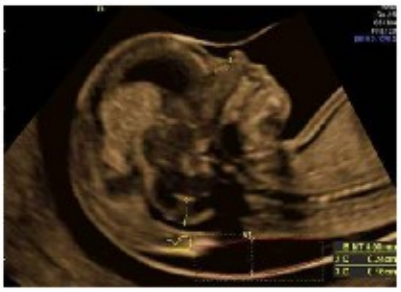
- **Maternal age related risk is multiplied by this ratio.**
- **Each test has predetermined value deemed abnormal (for 2nd trimester the threshold for downs in a women aged 35yr is 1:270) .**

ANALYTES	Normal karyotype	TRISOMY 21	TRISOMY 18	TRISOMY 13
Beta HCG (MoM)	1.0	2.0 **(increased)**	0.2 (Decreased)	0.5 (Decreased)
PAPP-A (MoM)	1.0	0.5 (Decreased)	0.2 (Decreased)	0.3 (Decreased)

In twin pregnancies the serum free markers are approximately double the singleton values , thus detection rate becomes 15 % lower . Hence NT as an isolated marker is used in multiple pregnancies.

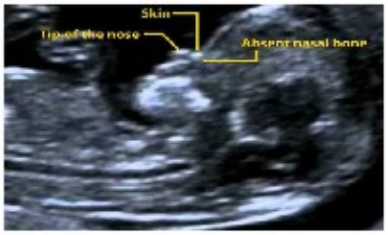
Nuchal translucency (11week to 14 week)

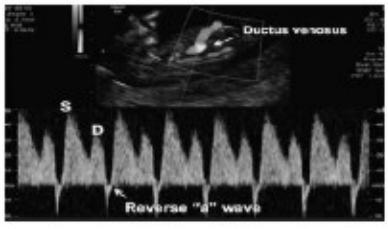
- Max thickness of the subcutaneous translucent area between the skin and soft tissue overlying fetal spine at back of neck
- NT if more than 3mm or exceeds 99th percentile it means abnormal and investigation required-
- Targeted sonography + fetal 2D echo + cell free DNA testing or prenatal diagnostic test (chorion villus sampling)



Additional USG markers in 1st Trimester for Down's Syndrome

- Absence of nasal bone /nasal bone hypoplasia
- Reversal of a wave of ductus venosus
- Tricuspid regurgitation





SECOND TRIMESTER SCREENING

Biochemical Test

Tests	Triple test	Quadruple test
Components	Serum Beta HCG Serum Alpha feto protein Serum Free estriol (UE3)	Serum Beta HCG Serum Alpha feto protein Serum Free estriol (UE3) Serum Inhibin A
Sample	Maternal serum	Maternal serum
Gestational age	15 to 21 weeks	15 to 21 weeks
Detection rate	69 %	81 to 85.8 %
comments	Less accurate as first trimester screening have increased accuracy	Most common 2nd trim screening. No benefit over 1st trim screening for trisomy 21 and 18 It is generally used if a) Women is not vigilant till 2nd trimester b) 1st trimester screening not available.

Genetic disorder	AFP	UE3	hCG	Inhibin A
Down syndrome	↓	↓	↑	↑
Trisomy 18	↓	↓↓	↓↓	↔
Trisomy 13	↔	↔	↔	↔

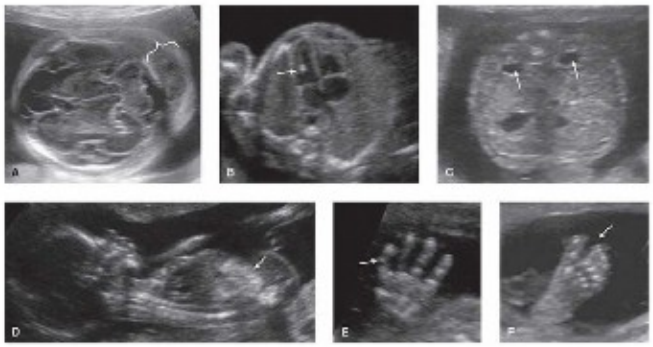
Biophysical Test

- Gestational age – 18 to 22 weeks
- Look for a) major abnormality b) soft markers/ minor abnormality
- ***Major markers*** **defined** as major structural abnormalities confirm risk of genetic syndromes
- ***Minor markers*** **as defined** are normal variants rather than fetal abnormalities and in absence of any aneuploidy, they do not affect the prognosis

Second-Trimester Sonographic Markers or "Soft Signs" Associated with Fetal Trisomy 21

Present in 10 % of unaffected pregnancies.

- Aberrant right subclavian artery
- Echogenic bowel
- Echogenic intracardiac focus
- Nasal bone absence or hypoplasia
- Nuchal fold thickening
- Short femur
- Short humerus
- Pyelactasis
- Ventriculomegaly (mild)



Cell-Free DNA Screening (Noninvasive screening test)

- Cell-free DNA -small amount of DNA that is released from the placenta.
- Can be done at any time after 9- 10 weeks'.
- Reporting takes 7 to 10 days
- Three types of assays- whole genome sequencing, chromosome selective or single nucleotide sequencing

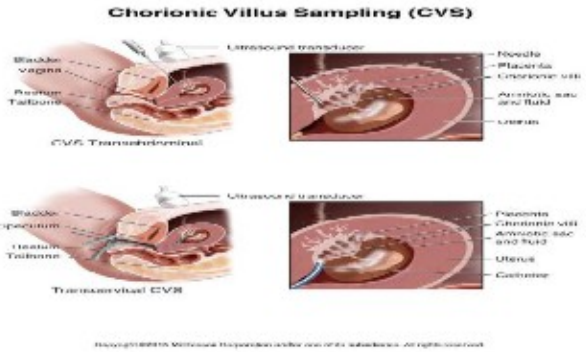
Indications of Cell Free Fetal DNA

- Maternal age ≥35 years
- History of a prior pregnancy with a trisomy
- Positive first trimester or second trimester analyte based screening test
- Sonogram with minor aneuploidy marker
- Parental balanced robertsonian translocation with increased risk of trisomy 13 or trisomy 21.

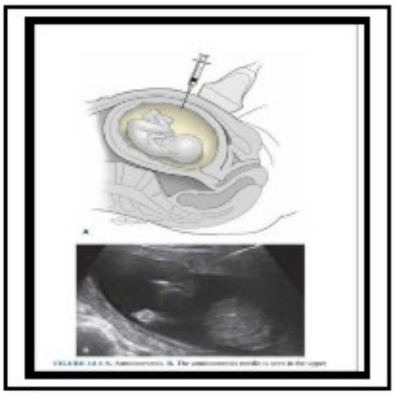
Prenatal Diagnostic Test

a) Chorionic villous sampling

- biopsy of chorionic villi
- Gestational age – 10 to 13 wk
- Advantages- results available early, so if termination needed can be planned on time.



Amniocentesis



- Most common prenatal diagnostic procedure
- Gestational age – 15 to 20 weeks
- Reporting time 7 to 10 days

Indications – a) diagnosis of fetal genetic disorders

b) Congenital infections

c)Assessment of fetal lung maturity

Complications a) loss rate- = 0.1 to 0.2 %

b) Amniotic fluid leakage - generally occurs within 48hr of procedure, fetal survival rate > 90 %

c) Transient vaginal spotting

d) Needle injuries to fetus

Foetal sampling / Cordocentesis/PUBS (percutaneous umbilical blood sampling)

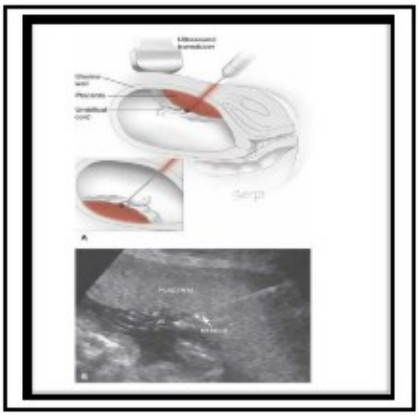
Indications –

a) Fetal anemias assessment

b) Assessment and treatment of platelet alloimmunization .

c) Fetal karyotype determination .

- Gestational age -18 to 20 wk

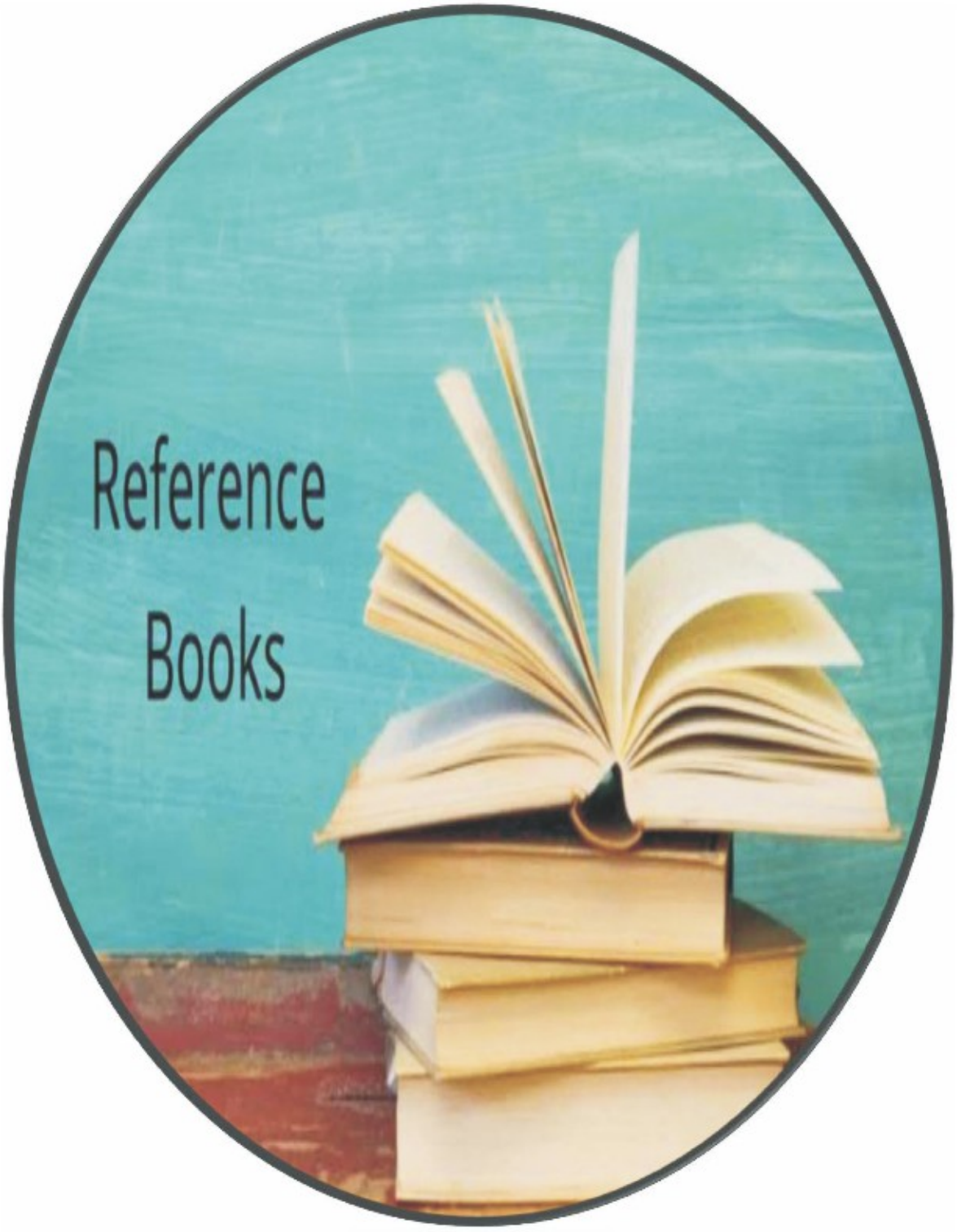


Advantage –

a) Chromosomal testing is quicker, i.e. 24 to 48 hours

	Chorionic Villus Sampling	**Amniocentesis**	**Cordocentesis (Fetal blood sampling)**
TIME	**Transcervical : 10 - 13 weeks**	**15 – 20 weeks (early 11 -14 weeks)**	**18 – 20 weeks**
MATERIALS FOR STUDY	**Trophoblast cells**	**Fetal fibroblasts fluid for biochemical study**	**Fetal white blood cells**
KARYOTYPE RESULT	**Direct preparation: 24 -48 hr Culture : 10 -14 days**	**Culture 7-10 days**	**Culture : 24 -48 hr.**

Fetal loss **Accuracy**	**1 -2 %** **Accurate**	**0.1 – 0.3 %** **Highly accurate**	**1 – 2 %** **Highly accurate**
Termination of pregnancy **if indicated** **Complication**	**1st trimester : safe** **Limb reduction defect.** **Oromandibular limb** **Hypogenesis.** **Vaginal bleeding.**	**2nd trimester : risky** **Vaginal bleeding 1 -2%** **Amniotic fluid leakage.**	**2nd trimester : risky** **Cord vessel bleeding (20-30%** **Fetal bradycardia (5-10 %).** **Williams OBSTETRICS 26th edition**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