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AOGD BULLETIN

Volume 21 I January 2022 I Monthly Issue 9

PROMOTE WOMEN'S HEALTH

STRONG WILL

QUALITY SKILL

Dedicated Issue:

"Critical Care in Obstetrics"

AOGD SECRETARIAT

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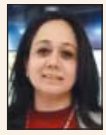

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Foreword

It gives me immense happiness and pride to write a foreword for this dedicated issue of **'Obstetric Critical Care'.** The very fact that a dedicated issue on this topic is being released speaks volumes about the progress made in this area and I am very satisfied to see that the seeds planted by Safdarjung Hospital Team have bloomed into a full plant.

Basic knowledge about critical care in obstetrics is the need of the hour. This is very important as Govt of India has mandated the setting up of dedicated Obstetric HDUs and ICUs in all public health facilities. Besides, the obstetric patient poses a unique challenge due to the physiological changes of pregnancy and the presence of the fetus which requires the obstetrician to remain at the helm of all decision making for the patient. Even in the private sector, these skills and knowledge are of utmost importance, to work in tandem with the critical care physician as the ultimate responsibility of the patient rests with the obstetrician only. I am sure all our readers will benefit tremendously from this issue as each topic has been written by experts who are actually working at ground level.

I am really happy that the Team AOGD under the leadership of Dr Achla Batra has provided a plethora of high level, academic events for its members and have truly lived up to this year's Theme of **"Promoting Women's Health by Strong Will and Quality Skills".** The quality of the AOGD Bulletin is also praiseworthy for which I applaud the untiring efforts of Dr Rekha Bharti and her entire Editorial Team. In fact, I have been told by many senior colleagues from different parts of the country that their post graduate students use these bulletins as a ready reference material. I am indeed a proud AOGDian and I am sure that the standards of our Society will keep rising with each passing year.

Best wishes to all our AOGD Members!

Dr Pratima Mittal
Chief Advisor, AOGD

From the President's Pen

Very warm Greetings to all!

On the joyous occasion of the New Year 2022, I extend my warm greetings and best wishes to all AOGD members. May the new dawn of the New Year reinvigorate the spirit of peace, prosperity and fraternity among us!

Two years into the COVID pandemic, and we are still witnessing waves after waves of COVID epidemic. But we are also proudly acknowledging the bravery and solidarity of our whole fraternity in fighting the disease and adapting to the new normal. Hopefully this New Year will be the light at end of tunnel and we will emerge victorious, but we must not forget to take precautions till then.

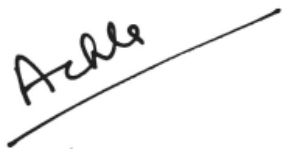
This New Year we have a new, more refined version of AOGD constitution, also it must be put on record that Dr Reva Tripathi chairperson of constitution committee has been the driving force that made us accomplish this marathon task within stipulated time.

New Year is also a time to reflect on what we have done and what more is to be done. Despite COVID restrictions, we did manage to accomplish a lot, not only on academic front but also in reaching out to public through the virtual media. Our PG forum is popular across the nation and so is our AOGD bulletin. We have started training in QI, PPIUD and respectful abortion care. One thing that was missing in our agenda was training in Research Methodology, therefore, we are starting a series on this subject to enable our members to effectively put forward the enormous data that they have collected.

This issue dedicated to **"Critical Care in Obstetrics"** is the need of hour. Critical care for pregnant women is different from nonpregnant women due to the physiological changes of pregnancy. I am sure it will be of great interest and of immense use to our readers. Wishing you all Happy Reading and Happy Lohri, Sankranti, Basant Panchami and Republic Day greetings!

"There was never a night or a problem that could defeat Sunrise or hope"

-B. Williams



Dr Achla Batra
President, AOGD (2021-2022)

From the Vice-President's Pen

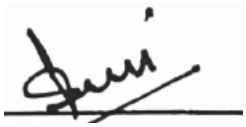
Dear Friends

This month our Readers will get an academic bonanza of a most crucial topic- **"Critical Care in Obstetrics".** Familiarity with the basics of diseases and conditions which can bring our obstetric patient to the ICU is of utmost importance for all of us.

Even if we don't have a dedicated HDU setting working in tandem with the intensivists can improve the outcome for our patients markedly. We highly recommend all our members to go through this issue and keep it safely for ready reckoning. Our Editorial Team under the proud leadership of Dr Rekha Bharti has worked very hard for this issue.

Hope you are all doing well as COVID is spreading its tentacles once more over our city and the cold wave is unabating in its severity. But this too shall pass and spring is around the corner!

Happy Reading



Dr Jyotsna Suri
Vice President, AOGD (2021-2022)

From the Secretary's Desk

Warm greetings to all !

Hope you all have been keeping safe and healthy. Glad to present before you this very important issue of our AOGD bulletin which deals with one of our committed areas of work as a part of our motto this year, '**Strong Will and Quality Skills- For Woman's Health**'. This third wave of COVID has not deterred us and we have continued our endeavours to work towards our motto. We continue to bring forth best of programs on latest developments in Obstetrics and Gynaecology for our members.

As part of imparting **'Quality Skills'** to our members we have been conducting various webinars and workshops on Critical care in Obstetrics through-out our tenure. Our chief advisor, Dr Pratima Mittal and Vice President, Dr Jyotsna Suri have even formulated a training programme in Obstetric Critical Care which is being implemented through one of the popular weekend courses conducted by ICOG.

As regards to this month's bulletin, I congratulate the editorial team, like always for another interesting and useful issue on **'Critical Care in Obstetrics'.** It aptly covers all the important aspects viz. approach to dysponea in pregnancy and hypertensive obstetric emergencies, Acute liver diseases, disseminated intravascular coagulation, obstetric shock and resuscitation of a pregnant woman. I am sure these evidence-based articles with practical tips and recent advances in field of critical care in obstetrics will be immensely useful for our readers especially the postgraduates and residents who deal with such emergencies first hand in all the institutes. The private practitioners also will be able to clear many doubts and may keep this document handy for help in their daily practice.

Happy reading to all,

Dr Monika Gupta
Secretary, AOGD (2021-2022)

From the Editor's Desk

Greetings from the editorial board!

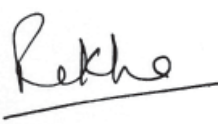
Wish you all a very Happy & Prosperous New Year 2022. We are pleased to release our first bulletin of this year on a very relevant issue **"Critical Care in Obstetrics".** Although pregnancy is considered a normal physiological state, it is a unique condition that can affect two lives at the same time. At many centers critically ill pregnant and postpartum women are managed by multidisciplinary approach with admission under critical care specialists or intensivists.

As we approach towards achieving global targets of reducing maternal mortality, it is essential that the obstetricians who are more verse with the physiology and conditions associated with pregnancy that lead to severe morbidity and mortality continue to be the in charge of women admitted in critical care units. It was difficult to cover all aspects of critical care obstetrics in one issue. Therefore, we have focused on few conditions that are more commonly encountered or are important part of obstetric practice.

We are grateful to Dr Pratima Mittal for writing foreword for this issue. She has been a driving force in implementing concept of Obstetric Critical Care unit at Safdarjung Hospital. We are also thankful to Dr Jyotsna Suri, incharge of critical care unit at Safdarjung Hospital for guiding us in selection of the topics.

We are thankful to all the authors for compiling and simplifying the respective articles for this issue of AOGD bulletin. **Hypertension** and associated emergency conditions are common cause of admission of pregnant women in the critical care units. Management of **Acute Liver Conditions** can be challenging as the differentiation of various conditions specific to pregnancy and coexisting with pregnancy may be difficult but crucial for optimizing maternal and fetal outcomes. **DIC in Pregnancy** that is secondary to many obstetric and medical complications contributes significantly to maternal morbidity and mortality if not identified and managed in time. Many unnecessary physician references can be avoided if physiological **Dyspnea in Pregnancy** can be differentiated from pathological dyspnea. At the same time, to avoid maternal and fetal complications, it is important to identify pathological dyspnea. Due to difference in the normal physiology, **Management of Obstetric Shock** needs different and more energetic approach compared to shock in non pregnant patients. **Resuscitation of Pregnant Women** is similar to resuscitation of non pregnant patients except for some modifications for relief of aortocaval compression due to gravid uterus. We hope you enjoy reading this bulletin.

Happy Reading!



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Hypertensive Emergencies in Obstetrics

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During pregnancy or postpartum period, hypertension is considered severe when the systolic blood pressure (BP) reaches 160 mm Hg or the diastolic BP reaches 110 mm Hg, or both on two occasions. When faced with severe hypertension, the diagnosis may need to be confirmed within a shorter interval (15 minutes) rather than 4 hours to facilitate timely antihypertensive therapy.

Table 1: Symptoms of Preeclapsia with Severe Features

SBP ≥ 160mH or DBP ≥ 110
• Headache (not relieved by regular analgesics
• Blurred vision
• Upper abdominal pain (Epigastric or right upper quadrant pain unresponsive to medications)
• Thrombocytopenia (platelet count <100 X 10^9/L (100,000)
• Elevated liver transaminases to twice normal concentration
• Renal insufficiency (S.cr.>1.1mg/dl or doubling in absence of other renal diseases
• Pulmonary edema

Goal of Treating Severe Acute Hypertension

Aim for BP is ≤135/85 mmHg, to decrease maternal complications of stroke or heart failure and Maternal stabilization if termination of pregnancy needed. *Systolic ≥ 160 is linked to maternal complications and diastolic ≥ 110 mm of Hg is linked with risk of Abruptio Placentae*

Risk Associated with Severe Hypertension

- Antepartum hemorrhage (Abruption)
- End organ damage
  - o Eclampsia: focal or generalized seizures
  - o Cerebrovascular accidents (hemorrhagic or ischemic stroke)
  - o Hypertensive encephalopathy
  - o Acute Heart Failure/ MI leading to Pulmonary edema
  - o Renal impairment
  - o Papilledema
- Fetal distress

Prerequisites for Ideal BP Measurement

- BP should ideally be measured by a mercury sphygmomanometer
- Patient should be sitting with back supported, legs uncrossed, arms supported at level of heart.
- Patient should refrain from smoking or drinking tea or coffee 30 minutes before measuring BP.
- Patient should not talk during measurement
- Patient should not tense the arm or clench the fist during measurement
- Bladder should be empty

*The first audible sound (Korotkoff I) is the systolic pressure and the disappearance of sound (Korotkoff V) is the diastolic pressure. However if sounds are audible with cuff deflated, commonly observed in pregnant ladies, then Korotkoff IV should be used.

Clinical Assessment and Examination of Patient

Assess consciousness; Monitor vitals; Chest auscultation; Check deep tendon reflex; Secure intravenous line; Catheterize for monitoring urine output; Monitor signs and symptoms of impending eclampsia / pulmonary oedema; Calculate gestational age.

Ancillary Investigations for Maternal Assessment

- Complete hemogram with platelet count with peripheral smear for hemolysis
- Kidney function test
- Liver function tests
- Urine albumin by dipstick & 24 hours urine protein Or Urine protein creatinine ratio
- Arterial blood gas analysis
- Electrocardiogram
- Fundus examination
- PT/INR
- Chest X-ray if indicated

Fetal Assessment

- Non stress test or cardiotocography
- Ultrasound biometry with color doppler once mother is stabilised, if conservative management is planned

Management

First Line Antihypertensive Therapy- Intravenous Labetalol or Intravenous Hydralazine or Oral Nifedipine, Fig 1.

Magnesium sulphate- Drug of choice for seizure prophylaxis but not recommended as antihypertensive agent

Transfer the Patient to Tertiary Care- For maternal & fetal monitoring

Intubation if required

Once treatment is initiated, we attempt to reduce mean arterial pressure by no more than 25% over two hours (10-20% in first hour then 10-15% in next hour) to achieve target blood pressure of 130 to 150 mm Hg systolic and 80-100 mm Hg diastolic. Aggressive lowering of BP below 120/80 mm Hg may be associated with decreased uteroplacental perfusion.

Timing of Delivery

In Preeclampsia with Severe Features (Table 1): < 26 weeks POG- Deliver; 26-34 weeks POG- Administer Corticosteroids if not previously administered and deliver; > 34 weeks POG- Deliver

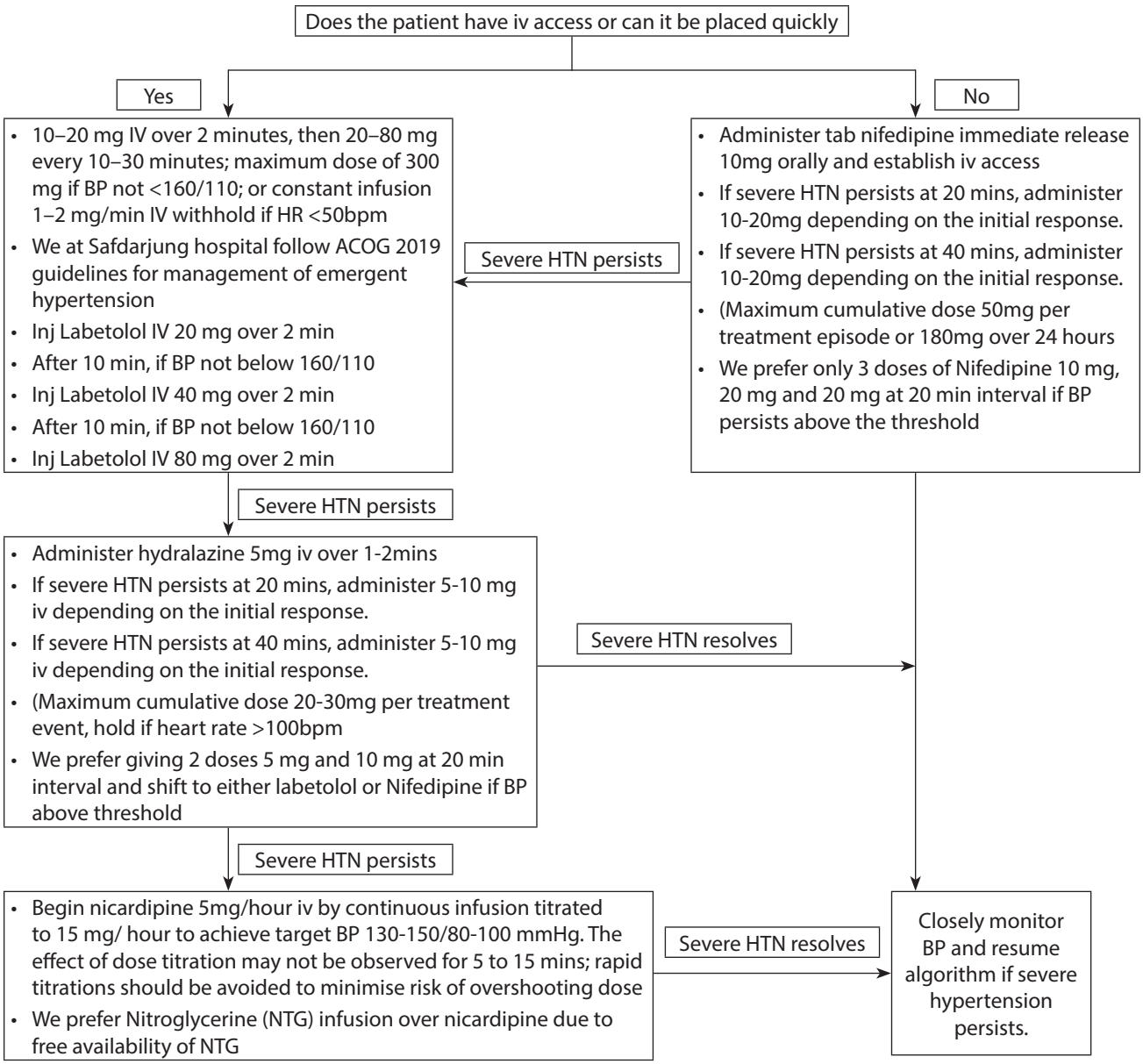

Fig 1: Management of Severe Hypertension

Deliver Immediately

Maternal indications: Inability to Control BP Using >3 Classes of Anti hypertensives; Persistent headaches, refractory to treatment; Epigastric pain or right upper quadrant pain unresponsive to repeat analgesics; Visual disturbances, motor deficit or altered sensorium; Stroke; Myocardial infarction; HELLP syndrome; New or worsening renal dysfunction (serum creatinine greater than 1.1 mg/dl or twice baseline); Pulmonary edema; Eclampsia; Suspected acute placental abruption or vaginal bleeding in the absence of placenta previa.

Fetal indications: Non reassuring fetal heart rate; Fetal death/ Congenitally anomalous fetus; Fetus before the period of viability; Persistent reversed end-diastolic flow in the umbilical artery

Complications

Eclampsia

The occurrence of a convulsion in association with pre-eclampsia syndrome complicates 1 in 100 to 1700 deliveries in low- and middle-income countries and is associated with 10% of maternal deaths. Management is aimed at aborting current convulsion, preventing further convulsion and safe and timely delivery. After initial stabilization (avoid injuries, maintain oxygenation and minimize aspiration, initiate magnesium sulfate, control blood pressure), give corticosteroids if gestation <34 weeks but do not delay delivery and plan delivery.

Magnesium Sulphate is given for Eclampsia Prophylaxis or Management of Eclampsia.

Pritchard Regime: Loading dose- 4 g of 20% solution- slow iv over 5 mins; f/b 10 g of 50% solution, 5 g each i.m. deep in the upper outer quadrant of each buttock (Addition of 1.0 mL of 2% lidocaine minimizes discomfort). Maintenance dose- Every 4 hourly, give 5 g of 50% solution IM deep in the upper outer quadrant of alternate buttock

Zuspan Regime (Intravenous Regime): Loading dose- 4 g IV (20%) slowly over 5-10 min; Maintenance dose- 1gm/hour given by an infusion pump

Maintenance dose is given if patellar reflex is present, respiratory rate > 12/min, and urine output during previous 4 h-exceeded 100 mL (25ml/hr). Serum monitoring of magnesium levels is expensive and has not been shown to be superior to clinical monitoring. Calcium gluconate 10% 10 ml over 10 minutes is antidote for Magnesium Sulphate toxicity. Vaginal delivery is preferred and Caesarean section is done only for obstetric indications and non responsive hypertension/recurrent seizures. Fluid overload should be avoided.

In the postpartum period shift of antihpertensives can be undertaken and magnesium sulphate is continued for 24 hours after delivery.

Contraindications of MgSO4- Mysathenia gravis, Hypocalcemia, moderate to severe renal, failure, cardiac ischemia, heart block, myocarditis.

Recurrent Seizure

Give Magnesium sulfate- 20% 2 gm IV; or Diazepam – 5 -10 mg I/V every 5 -10 mins at a rate ≤5 mg/min and maximum dose 30 mg; or Lorazepam- 4 mg IV at maximum rate of 2 mg/minute or Midazolam - 1 to 2 mg bolus given i.v at a rate of 2 mg/min.

Resistant Hypertension

Consult with a cardiologist or critical care subspecialist for second-line antihypertensives

Nitroglycerine (2nd line antihypertensive)

- 1 Ampoule of NTG= 5 ml (5 mg/ml) = 25 mg
- Preparation: 2 amp (10 ml) of NTG + 40 ml DNS/D5 = 50 ml solution (1mg/ml)
- Start at 5 mcg/min (0.3 ml/hr infusion rate), increase by 5 mcg/min every 3-5 minutes
- Maximum dose of 100 mcg/min
- Drug of choice in Pulmonary Edema

Other Second line Drug: Nicardipine, esmolol administered by infusion pump; Sodium nitroprusside is reserved for extreme emergencies

Once BP is stabilised start oral antihypertensives: Tab. Labetelol 100 mg TDS (maximum 2400 mg) (First Line): or Tab. Methyldopa 250 mg TDS (maximum 2grams)

Monitoring and Follow Up

- Blood pressure monitoring should continue every 10 min for first hour, every 15 min for second hour, every 30 min for third hour and hourly for four hours (for patients not in labour; supposed to be done more frequently for patients in labour)
- Vital signs (PR, RR, SPO2, DTR and Mental status) every 15-30 minutes until stable and then hourly
- Input and output monitoring (to avoid fluid overload)
- Postpartum- Continue antihypertensive treatment, consider reducing the treatment if BP < 140/90

Acute Pulmonary Edema with Hypertension

For urgent reduction of critically high blood pressure give intravenous antihypertensive agent but *avoid Labetalol*. Nitroglycerine (glyceryltrinitrate) is the drug of choice in pre-eclampsia associated with pulmonary edema and consider Positive pressure ventilation; NIV in selected cases or Invasive mechanical ventilation.

Clinical Presentation: Pulmonary edema usually presents with a characteristic clinical picture of severe dyspnea with production of pink frothy sputum, diaphoresis and cyanosis. Physical examination reveals a low-flow state, S3 gallop, jugular venous distention and fine crepitant rales in all the lung fields on auscultation.

Diagnostic testing: The diagnosis of pulmonary edema is made based on symptoms and clinical signs are found through history taking, physical examination, ECG, chest X-ray, echocardiography and laboratory tests including blood gas analysis and specific biomarkers.

Ultrasound- USG of lung is an important bedside tool to diagnose pulmonary edema (B lines) and also to assess fluid status of the patient (IVC collapsibility)

Arterial Blood Gas, CBC, KFT, LFT, and INR (Infection, renal or liver failure, anemia or electrolyte abnormalities can be identified which may precipitate or exacerbate pulmonary edema).

Echocardiography- It should be performed to confirm suspected cardiac lesions such as valve dysfunction, cardiomyopathy, ventricular wall rupture or tamponade.

Management

The main aim is to relieve symptoms and to restore haemodynamic stability and tissue perfusion. *Secure airway and start oxygen, Non invasive ventilation-* to improve oxygenation, decrease the work of breathing and increase cardiac output. Continuous Positive Airways Pressure (CPAP) provides a constant level of positive airways pressure preventing alveolar collapse. **NIV is contraindicated** when immediate endotracheal intubation is indicated; respiratory arrest or inadequate spontaneous ventilation is present; there is worsening life threatening hypoxia; and in unconscious patient unable to protect own airway.

Following initial management, treatment focuses on 3 main goals: (1) Reduction of pulmonary venous return (preload reduction) (2) Reduction of systemic vascular resistance (afterload reduction) and in some cases, (3) Inotropic support. Avoiding aortocaval compression is essential.

Preload Reduction: Loop diuretics reduce preload but high doses may have detrimental effect in preeclamptic women. They may cause dehydration, hyponatraemia and hypotension. Give s*mall intravenous* initial bolus of *furosemide* 20–40 mg over 2 min, repeated dose of 40–60 mg is administered after approximately 30 min, the maximum dose is 120 mg/hour.

Afterload Reduction: These agents have positive physiological effects by off-loading the heart through their venous and/or arteriolar vasodilatory effects causing a reduction in pre-load and/or after-load. ***Nitroglycerin*** *(glyceryl trinitrate) is recommended as the drug of choice in pre-eclampsia associated with pulmonary oedema* (level 3 evidence). **Nitroprusside** reduces preload and afterload. But, due to the risk of fetal cyanide poisoning by its metabolites thiocyanate and cyanide, it should only be used in pregnancy when all other interventions have failed. Start infusion at 0.3 mcg/Kg/min and titrate up to 5mcg/Kg/min with invasive blood pressure monitoring. **Nesiritide** is both an arterial and veno dilator. It is pregnancy category C drug and should be used only if no other alternative is available.

If hypertension persists despite the combination of nitroglycerin or sodium nitroprusside and furosemide, then a calcium channel antagonist such as **nifedipine or nicardipine** may be considered (especially if diastolic dysfunction is diagnosed). **Hydralazine** (level 1++ evidence) may also be used to control BP; however, reflex tachycardia may cause deterioration of pulmonary edema. **Intravenous morphine** 2–3 mg is given as a venodilator and anxiolytic, to be used with caution as nausea and hypopnea may occur.

High dependency care and close observation are essential: Continuous monitoring of vital signs, serial monitoring of respiration, cardiac, renal and haematological function and assessment of fetal wellbeing with multidisciplinary planning for safe birth is essential if acute pulmonary oedema occurs antenatally.

Inotropes: are given in case of hypotension or signs of end organ hypoperfusion despite use of vasodilators/

diuretics. They should be commenced early once the need is recognized and stopped as soon as adequate tissue perfusion is achieved. Their use is associated with increased mortality, as they increase cardiac oxygen demand and myocardial injury. **Dobutamine** is the first choice agent, infusion is commenced at 2-3 mcg/kg/min and increased as required, *Should be avoided in moderate to severe hypotension, SBP <80 mmHg*. **Dopamine:** The vascular and myocardial receptor effects of dopamine, are dose dependent. Moderate and high dosages are arrhythmogenic and increase myocardial oxygen demand. Therefore, use these dosages only in patients with Cardiogenic pulmonary edema who cannot tolerate dobutamine because of severe hypotension (eg, systolic blood pressure 60-80 mm Hg).

Vassopressors: **Norepinephrine**, is generally reserved for patients with profound hypotension (e.g., systolic blood pressure < 60 mm Hg). After blood pressure is restored, add other medications to maintain cardiac output.

Neurological Complication

Posterior reversible leukoencephalopathy syndrome (PRES) and stroke are the most serious neurological complications associated with hypertensive emergency.

PRES is arises due to acute hypertension and endothelial damage leading to vasogenic edema. It is characterized by forced leakage of serum through capillary walls and into the brain interstitium with preferential involvement of the posterior brain.

Clinical Presentation

- Headache which is usually non localized, constant, moderate to severe and refractory to analgesia
- Visual disturbances mostly perception abnormalities like auras, hemianopia, visual neglect, visual hallucinations and cortical blindness.
- Altered consciousness ranging from mild somnolence to confusion progressing to coma in extreme cases.
- Seizures that are generally tonic clonic type but may begin focally. Status epilepticus might also be seen.

Diagnosis is made by combination of clinical features and neuroimaging (either CT or MRI). Typical features include white matter edema in the posterior cerebral hemisphere. Involvement of cerebellum and brainstem are also common. Lesions of the frontal lobe do occur but edema is also present in the posterior circulation territories. The superior and frontal gyrus is preferentially affected. Although subcortical white matter is primarily involved, basal ganglia and cortex are often involved.

Treatment involves management of blood pressure with antihypertensive drugs and magnesium sulphate to prevent eclampsia and cerebral edema. Immediate delivery should be undertaken by induction of labour or cesarean. Role of mannitol is limited and should be considered only after neurology opinion.

Conclusion

Hypertensive emergency should be treated immediately to prevent further maternal end-organ damage and fetal morbidity and mortality. First line antihypertensive therapy should be initiated immediately to improve fetal and maternal prognosis.

Suggested Reading

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Acute Liver Diseases: Challenges in Management

Zeba Khanam[1], Harsha Gaikwad[2]
[1]Senior Resident, [2]Director Professor, VMMC & Safdajung Hospital, New Delhi

The liver is an important organ of the body responsible for metabolic, immunogenic, digestive, detoxification, and storage functions. Three percent of pregnant women develop abnormal liver functions during pregnancy. Some coincident hepatobiliary diseases can get worsened during pregnancy. Other liver diseases may be specific to pregnancy or unrelated to it. (Table.1)

Physiology of Hepatobiliary System in Pregnancy

The liver blood flow is unaltered throughout the pregnancy. The liver size remains similar to the pre-pregnant size. However, there is an upward displacement of the liver with uterine enlargement.

Table 1: Acute liver diseases during pregnancy

Liver diseases specific to pregnancy	Intrahepatic cholestasis of pregnancy (IHCP); HELLP (hemolysis, elevated enzymes, and low platelets) syndrome; Hyperemesis gravidarum; Acute fatty liver of pregnancy (AFLP); Preeclampsia with severe features.
Diseases exacerbated by pregnancy	Gall stones; Vascular diseases (Budd chiari syndrome, portal vein thrombosis)
Disease not related to pregnancy	Acute viral hepatitis (Hepatitis A,B,C,E virus; Herpes simplex virus; Others); Drugs related hepatic injury; Sepsis associated cholestasis

The levels of blood urea nitrogen, albumin, and total proteins decrease due to the expansion of blood volume. Aminotransferase (alanine aminotransferase-ALT, aspartate aminotransferase-AST), gamma-glutamyl transpeptidase, and bilirubin levels are similar to the pre-pregnancy levels or 20% less than the average non-pregnant values. Alkaline phosphatase levels rise three times the normal. The levels of triglycerides and cholesterol also increase during pregnancy. Skin lesions in form of spider angiomas and palmar erythema are common due to increased estrogen levels. Spider angiomas and palmer erythema usually resolve after delivery.

Laboratory Tests for Evaluation of Liver Disorders in Pregnancy

In women with a history of prior pregnancy-related liver disease, chronic or pregnancy-induced hypertension, presence of risk factors for liver disease (metabolic syndrome, alcoholism), and viral hepatitis certain baseline liver function tests should be done. These hepatobiliary tests include serum aminotransferases (ALT/AST), alkaline phosphatase (ALP), total bilirubin levels, Prothrombin time (PT)/ international normalized ratio (INR), and serum albumin. Other important tests to consider are complete blood counts, serum creatinine, electrolytes, and blood glucose testing.

Evaluation of Liver Disorders in Pregnancy without Liver Failure

The evaluation of liver disorders in pregnancy should begin with a comprehensive history taking and physical examination. Laboratory studies and liver imaging are important adjuncts in reaching a diagnosis.

History of onset of severe nausea and vomiting before 20 weeks of gestation is suggestive of hyperemesis gravidarum. New-onset hypertension at ≥20 weeks may suggest preeclampsia/HELLP syndrome. The presence of nausea, vomiting, abdominal pain and headache in the third trimester is suggestive of AFLP. History of exposure to hepatotoxins (drugs, supplements, alcohol) should be elicited. History of liver disease in the previous pregnancy is important. History of pruritus and jaundice should be noted. Dyslipidemia and obesity are important risk factors for liver disease.

Physical examination during pregnancy may not be necessarily suggestive of liver disease. Liver enlargement may be missed with advancing gestation. The presence of ascites and jaundice should be noted.

Ultrasound with/without Doppler may be useful in detecting liver abnormalities. In conditions where ultrasound cannot detect the liver pathology (as in biliary obstruction or cholangiopathy), non-contrast MRI is useful. Further evaluation depends upon the type of liver injury.

If the pattern of liver injury is **hepatocellular** (disproportionate rise in serum aminotransferases as compared to ALP; seen in drug-induced hepatic injury, viral hepatitis, non-alcoholic fatty liver,

alcohol-associated liver disease, autoimmune hepatitis, and most pregnancy-related liver diseases), the following tests may be advised:

a. Viral hepatitis- Immunoglobulin M (IgM) anti-hepatitis A virus; Hepatitis B surface antigen (HbsAg); IgM antibody to hepatitis B core antigen; antibody to HbsAg; Anti-hepatitis C virus antibody with reflex to hepatitis C viral RNA; IgM anti-hepatitis E virus; Herpes simplex virus DNA by polymerase chain reaction; Cytomegalovirus DNA assay; Epstein-Barr virus serology.
b. Autoimmune hepatitis- Antinuclear antibodies, anti-smooth muscle antibodies, immunoglobulin G
c. Intrahepatic cholestasis of pregnancy- Total bile acid concentration
d. Wilson disease- Ceruloplasmin

In cases of the **cholestatic** pattern of liver injury (disproportionate rise in serum ALP as compared to serum aminotransferases; seen in drugs-related liver injury, primary biliary cholangitis, and primary sclerosing cholangitis), the following tests may be recommended:

a. Primary biliary cholangitis: Antimitochondrial antibody
b. Primary sclerosing cholangitis: Non-contrast magnetic resonance cholangiopancreatography

It is important to note that bilirubin levels should not be used to differentiate between hepatocellular and cholestatic liver injury, as it may be raised in both of these injury patterns. However, in cases of pregnancy-related liver injury, bilirubin levels are usually normal.

Role of Liver Biopsy in Diagnosing Liver Diseases During Pregnancy

A biopsy is usually not required for liver diseases that are pregnancy-specific. It should be only done when other tests fail to diagnose the cause of liver disease. A transjugular approach is advocated with a deranged coagulation profile.

Acute Liver Failure in Pregnancy

Acute liver failure during pregnancy is characterized by severe liver injury in form of a rise in serum aminotransferases more than 10 times the upper normal limit of normal, encephalopathy, and coagulopathy. Such patients require specialists in materno-fetal medicine and hepatology. They are best managed at a center with a liver transplant facility.

The causes of acute liver failure in pregnancy can be pregnancy or non-pregnancy-related. Pregnancy-related liver failure is generally seen after 20 weeks of gestation. These include AFLP, preeclampsia with severe features, and HELLP syndrome. Non-pregnancy-related acute liver failure may be seen any time during pregnancy. The common causes are acute viral hepatitis, drug-induced liver injury, and ischemic hepatitis.

The epidemiology, presentation, diagnosis, treatment, and postpartum management of pregnancy-associated liver diseases are summarized in Table 2.

Table 2: Pregnancy specific acute liver diseases

Acute fatty liver of pregnancy (AFLP)- The most important cause of liver failure in pregnancy	**Preeclampsia with severe features/ eclampsia**	**HELLP syndrome**	**Hyperemesis gravidarum**	**Intrahepatic cholestasis of pregnancy (IHCP)**
Incidence				
1 in 7000-20,000 pregnancies. The recurrence rate is unknown, however, may be seen in the next pregnancy.	5-10%. 90% cases present in late term or postpartum period. Recurrence rate of 25-75% is seen in next pregnancy with early onset severe preeclampsia.	HELLP syndrome is seen in 0.1- 1 % of pregnant women and in 1-2% women with preeclampsia. Recurrence rate of 7% seen in subsequent pregnancy.	0.3-3% of pregnancies.[2] Recurrence seen in subsequent pregnancy with similar severity	<1 to 27.6%. Geographical variations are seen. Seen more in winters. The recurrence rate is between 60-70%

Risk Factors				
Fetal long-chain 3-hydroxy acyl CoA dehydrogenase (LCHAD) deficiency. A previous episode of AFLP. Multiple gestations. Preeclampsia with HELLP syndrome. Male fetus. Low body mass index (<20 kg/m^2). Nulliparity.	History of preeclampsia, placental insufficiency. Preexisting maternal conditions as pregestational diabetes, chronic hypertension, systemic lupus erythematosus, antiphospholipid antibody syndrome, obesity, and chronic kidney disease. Multiple pregnancies. Nulliparity. Positive family history in a first-degree relative. Personal history of preterm birth and low birth weight. Advanced maternal age. Use of assisted reproductive technology.	Previous history of preeclampsia. Genetic factors. Nulliparity is not a risk factor as in preeclampsia.	Western world. Urban dwellers. Young Primigravida. History of motion sickness or migraines. Supertasters. Multiple gestations. Similar symptoms in a previous pregnancy. Hydatiform mole. Acid reflux. Other gastrointestinal disorders. Female fetus. Genetic association. Nonusage of multivitamins before pregnancy. **Protective factors**- Alcohol and cigarette use	Multiple pregnancies. Chronic hepatitis C. Prior family history of IHCP. Advanced maternal age. Increased risk in first degree relatives.
Pathogenesis				
Defect in maternal-fetal fatty acid metabolism leads to accumulation of intermediate long chain fatty acid metabolites into maternal hepatocytes. Deficiency of fetal LCHAD enzyme due to homozygous G1528C mutations (also associated with the development of HELLP syndrome) is the most common enzyme defect. Other defective enzymes are Short-chain acyl-CoA dehydrogenase, Medium-chain acyl-CoA dehydrogenase, Carnitine palmitoyltransferase deficiency, Mitochondrial trifunction protein deficiency.	Defective deep placentation and failure of spiral artery remodeling. The pathologic placenta releases anti-angiogenic factors which cause maternal vascular inflammation, endothelial dysfunction leading to hypertension and proteinuria.	Pathogenesis is unclear. May have a similar origin as preeclampsia but with a divergence to a more severe hepatic inflammation and greater activation of the coagulation cascade. The microangiopathy may be secondary to complement activation. Fetal LCHAD deficiency is seen in < 2% cases.	Multifactorial pathogenesis. Possible etiological factors are: Elevated serum estrogen, progesterone, and human Chorionic Gonadotrophins levels. Gastric Motility disturbance. H. pylori infection. Association with GDF15 and IGFBP7 genes. Zinc and vitamin B6 deficiency.	Possible etiological factors are: ABCB4 gene association in familial IHCP. Other responsible genes are ABCB11, ATP8B1, ABCC2, NR1H4. Rise in serum estrogen and progesterone. Low selenium levels. Low Vitamin D levels. Underlying liver diseases.

Clinical Features				
Presents between 30-38 weeks of gestation (usually in the third trimester), but maybe seen as early as 22 weeks and as late as 96 hours after delivery. Initial symptoms are non-specific (nausea and vomiting in 50-80% cases, fever in 25-30% cases, abdominal pain malaise, headache, anorexia). HELLP syndrome is seen in 20% and preeclampsia in 20-40% of women with AFLP. Acute liver failure presents as jaundice, ascites, encephalopathy, disseminated intravascular coagulation, hypoglycemia leading to multi-organ failure and death. Can also be associated with renal dysfunction, diabetes insipidus (due to decreased clearance of vasopressinase by liver) and acute pancreatitis. There is metabolic acidosis and maternal hypovolemia leading to decreased uteroplacental function and perfusion and fetal distress. Hypertension is seen in 50% of mothers.	The onset of severe preeclampsia is usually in the second half of pregnancy (mostly in the third trimester). May also be seen in the postpartum period (usually within 48hours). Severe preeclampsia is characterized by persistent and/or severe headache, visual abnormalities, upper abdominal pain, altered mental state, new-onset dyspnea, and orthopnea. Other symptoms include mental status changes, stroke, pulmonary edema, generalized hyperreflexia, grand-mal seizures (eclampsia), oliguria, peripheral edema and abruption. Hypertension is seen in 100% of cases. Fever is not seen.	Onset of HELLP syndrome is in second half of pregnancy (usually in third trimester). May also be seen in postpartum period (usually within 48hours). The onset is rapid and leads to progressive worsening of the maternal condition. HELLP syndrome represents preeclampsia with severe features with predominant liver abnormality and thrombocytopenia. >80% of women have hypertension and/or proteinuria. In 15% of patients, hypertension is absent. The most common symptom is abdominal pain and tenderness in the epigastrium/right upper quadrant/below the sternum. Nausea, vomiting, and malaise are common. Jaundice is seen in 5-10% of cases. Headaches, visual changes may occur but are uncommon. Liver rupture is rare. Fever is not seen. Severe morbidity may develop in form of disseminated intravascular coagulation, abruption, acute kidney injury, pulmonary edema, liver hematoma, and retinal detachment. It is unusual to find thrombocytopenia-related bleeding.	Nausea and vomiting start at 5-6 weeks of gestation, peak at 9 weeks, and subsides by 16-20 weeks. In 15-20% of women, it may persist till the third trimester and in 5% until delivery. Weight loss >5% with persistent vomiting and ketonuria unrelated to other causes is pathognomic of hyperemesis gravidarum. Orthostatic hypotension. Tachycardia. Low volume pulse. Hypersalivation/ Ptyalism. New-onset hypertension is absent. Severity scoring system- Mother risk-PUQE scoring index and Rhodes index.	Symptoms first appear during the late second and third trimester. Transient first trimester symptoms are seen in ovarian hyperstimulation syndrome. Pruritus is the first and the cardinal sign. It starts at palms and soles then becomes generalized and worsens at night. Right upper quadrant pain. Poor appetite. Sleep deprivation. Steatorrhea. No primary skin lesions are seen. Prurigo nodules and excoriation marks are secondary skin lesions.
Laboratory Findings				
Serum aminotransferases modestly elevated, up to 500 IU/L. Serum bilirubin- raised. Serum glucose – low. Serum creatinine- high (normal: 0.4-0.8 mg/dL). White blood counts- high (normal pregnancy range 9000-15000 cells/microL).	Serum bilirubin- raised but not as high as AFLP. Serum glucose- normal, low, or high. Serum creatinine- raised (>1.1 mg/dL or 2 times the baseline value) but less as compared to AFLP.	**Tennessee classification** Hemolysis (suggested by at least 2 of the 4:- schistocytes and burr cells in peripheral smears; serum bilirubin ≥1.2 mg/dL; low serum haptoglobulin ≤25 mg/dL or LDH ≥2 times the upper level of normal; severe anaemia not related to blood loss)	Abnormal liver function tests are seen in 50% of women (Rise in ALT is more than the rise in AST. However, both of these are only mildly elevated; Serum Bilirubin levels are usually normal. Rarely	Serum total bile acids- Raised; present in >90% affected cases and the first test to get deranged. Serum Cholic/ chenodeoxycholic acid ratio - raised. Total bilirubin- raised in 14-25% cases, but rarely >6mg/dL.

Ammonia levels- high. (useful in acute liver failure with ALT ≥5 times the normal values). Urate levels – high. PT/aPTT/INR- prolonged. Thrombin time- raised. Antithrombin – low. Platelet- low. Fibrinogen- low (<300 mg/dL). Fragmented RBCs and burr cells Proteinuria + Cholesterol- low. Serum lipase and amylase- raised with acute pancreatitis.	Serum Fibrinogen levels reduced but never <300 mg/dL in absence of massive hemorrhage. PT/aPTT/INR- usually not affected except in massive hemorrhage. Proteinuria ≥3g/24 hr or a random protein creatinine ratio of ≥ 0.3. Platelet count <150000/microL (10%). Hemolysis- schistocytes, helmet cells. Lactate dehydrogenase (LDH)-raised due to hemolysis or liver disorder. Hematocrit- raised. Transaminases- elevated (> 2 times upper limit for normal). Serum uric acid- raised. Other important findings- Raised cardiac troponin I, neutrophilia, hypocalciuria.	Elevated liver enzymes (AST or ALT ≥2 times the upper level of normal) Low platelets (<100,000 cells/microL) Those who do not meet all the 3 criteria have **partial HELLP syndrome.** **Mississippi sub-classification of HELLP syndrome** Class 1 – Platelet count ≤50,000 cells/microL plus LDH >600 IU/L and AST or ALT ≥70 IU/L; Class 2 – Platelet count >50,000 but ≤100,000 cells/microL plus LDH >600 IU/L and AST or ALT ≥70 IU/L; Class 3 – Platelet count >100,000 but ≤150,000 cells/microL plus LDH >600 IU/L and AST or ALT ≥40 IU/L. **ACOG criteria for diagnosis of HELLP syndrome:** LDH ≥600 IU/L**, &** AST and ALT elevated more than twice the upper limit of normal, **&** Platelet count <100,000 cells/microL.[3]	exceeds 4 mg/dL). Urine ketones- positive. Blood urea nitrogen – raised. Urine specific gravity- raised. Serum creatinine- raised or normal. Serum amylase/ lipase – raised in 10-15% cases. Hypokalemia. Hypochloremic metabolic acidosis. Serum calcium -reduced. Serum magnesium- reduced. Ketosis. Hematocrit- raised. Transient Hyperthyroidism.	Serum aminotransferases are raised in 60% cases, usually <2 times the upper limit of normal but may reach 1000 U/L. Serum alkaline phosphatase- raised but not specific. Serum gamma-glutamyl transpeptidase- normal or elevated (30%). PT Normal. May get prolonged with cholestyramine use.
Radiological imaging				
Uncertain role. Ultrasonography and MRI may show findings of fatty infiltration of liver.	CT scans in delivered patients may depict signs of posterior reversible leukoencephalopathy syndrome in severe hypertension. Fetal sonography and Doppler velocimetry can detect fetal growth restriction, oligohydramnios, hydrops, uteroplacental insufficiency Echocardiography of the mother may show decreased left ventricular function.	CT scans in delivered patients may depict signs of posterior reversible leukoencephalopathy syndrome in severe hypertension. Fetal sonography and Doppler velocimetry can detect fetal growth restriction, oligohydramnios, hydrops, uteroplacental insufficiency Echocardiography of the mother may show decreased left ventricular function.	Ultrasound should be done to confirm fetal cardiac activity, multiple pregnancies, molar pregnancy. Ultrasound of the liver may be advised.	Ultrasound of liver is grossly normal. Routine fetal sonography is advised.

Histopathology				
A biopsy is usually not needed for diagnosis. There is microvesicular fatty infiltration of hepatocytes with a foamy nucleus in the central and mid zonal parts of the liver lobule. There is periportal sparing. Cells stain positive for oil red O.	Biopsy not done. The placenta shows acute atherosis, shallow cytotrophoblastic invasion of spiral arteries. Placental infarcts and villous hypoplasia are also seen. Kidney- Glomerular endotheliosis	Biopsy not done. In addition to organ-specific histopathological findings of severe preeclampsia, the liver may show microvascular fibrin deposition, neutrophilic infiltrate fatty infiltration, lobular necrosis, and periportal hemorrhage.	Biopsy not done. Hepatic necrosis with cell drop outs, steatosis, and centrilobular vacuolation, and bile plugs are seen.	Biopsy not done for diagnosis. Cholestasis is seen without inflammation. Bile plugs are seen in canaliculi in zone 3 of the liver. Portal tracts are unaffected.
Diagnosis				
Diagnosis of AFLP does not exclude a diagnosis of other pregnancy-related liver diseases. SWANSEA criteria for diagnosis of AFLP include signs and symptoms, laboratory and imaging, and biopsy criteria.[4]	New onset of hypertension (≥160/110 mmHg) with/without proteinuria and significant end-organ dysfunction after 20 weeks of gestation or postpartum in a previously normotensive woman is severe preeclampsia.	Diagnosis is usually based on laboratory findings	Persistent omitting with ketosis and loss of >5% body weight in absence of other causes.	presence of pruritus associated with elevated total serum bile acid levels, elevated aminotransferases, or both, and the absence of diseases that may produce similar laboratory findings and symptoms. Severe cholestasis is consistently defined as bile acids over 40 micromol/L.
Treatment				
A multidisciplinary team of maternal-fetal medicine specialists, anesthetists, hepatologists and neonatologists should manage such cases. There should be an availability of a blood bank. Prompt delivery irrespective of gestational age is the dictum in AFLP. A MELD (Model for End-stage Liver disease) score of ≥30 suggests an increased risk of complications. Monitoring should be done by mental status assessment, pulse oximetry, urine output status. Mechanical ventilation may be needed for	For pregnancies ≥34+0 weeks- Delivery should be done. Between 23-34 weeks of gestation delivery is indicated with unstable maternal/ fetal condition, preterm labour, or membrane rupture. Expectant management may be given to allow for antenatal steroid administration and fetal lung maturity only if the maternofetal condition is reassuring. Measure blood pressure frequently. Give anti-hypertensives accordingly.	MgSO4 is started for seizure prophylaxis if severe hypertension is present. Severe hypertension should be treated with anti-hypertensives. If gestational age is below the limit of fetal viability or ≥34+0 weeks- deliver after maternal stabilization. If gestational age is above the limit of fetal viability but <34+0 weeks- administer steroid cover to mother for fetal lung maturation under intense feto-maternal monitoring. Plan immediate maternal stabilization and termination of pregnancy in cases of nonreassuring fetal heart pattern, fetal death, abruptio placenta, pulmonary edema, eclampsia, hepatic bleeding, stroke, acute kidney injury, and disseminated intravascular coagulation.	Patients require inpatient treatment with intravenous fluid replacement and anti-emetics (prochlorperazine, diphenhydramine, metoclopramide, ondansetron). Correction of electrolytes and abnormal acid-base balance is required. Thiamine is added to intravenous fluids to prevent Wernicke's encephalopathy. A short period of nil per oral may be followed by slow reintroduction of oral intake with liquid, bland, and low-fat foods.	Pruritus usually precedes the rise in serum bile acids by several weeks. Total bile acid and aminotransferase levels should be repeated weekly if they are initially normal. Ursodeoxycholic acid is the preferred treatment for pruritus. In refractory cases, S-adenosyl methionine, cholestyramine, or rifampin may be used but the evidence is lacking in their support. Antihistaminics (hydroxyzine, Chlorpheniramine), and lactocalamine lotion may also be

adult respiratory distress syndrome. Blood sugars are maintained above 65 mg/dL. If required, D10 continuous infusion may be used. Platelet counts/ PT/ INR/aPTT, fibrinogen levels should be measured 6-8 hourly. In the setting of coagulopathy, a liver transplant may be required. Disseminated intravascular coagulation should be managed according to protocol. Fetal monitoring- continuous fetal heart monitoring should be done. Consider inj MgSO4 at <32 weeks for fetal neuroprotection. Delivery should be accomplished within 24 hours of symptoms onset. Cervical ripening agents may be used. If delivery has not occurred by 24 hours, expedited delivery by cesarean section may be needed.	Give MgSO4 for the prevention of seizures. Monitor input and output. Serum biochemistry is done 6-12 hourly Fetal monitoring can be done by ultrasound assessment of liquor, fetal weight, and Doppler indices. Continuous fetal heart rate tracings should be taken out during labour. Vaginal delivery is preferred. Cesarean delivery should be reserved for obstetric indications.	With severe epigastric pain or right upper quadrant pain and/or liver enzymes being highly raised, an emergent ultrasonography or other relevant imaging should be done to rule out hepatic bleeding.	Glucocorticoids can be added in cases of refractory vomiting. The role of enteral feeding or parenteral nutrition is not clear. Enteral feeding may be started when women are unable to maintain weight due to vomiting despite medications.	tried for pruritus. Fetal monitoring is done by modified biophysical profile twice weekly, biometry fortnightly. Biophysical profile score and daily kicks counts are not useful for detecting uteroplacental insufficiency as intrauterine death is sudden in IHCP. Termination of pregnancy is recommended between 37-38+0 weeks if no other indications for early delivery are present. Delivery may be conducted at 36+0 weeks if total bile acid levels are ≥100micromol/L. In the presence of excruciating and unremitting maternal pruritus despite pharmacotherapy, worsening hepatic functions, or a history of intrauterine demise before 36 weeks, delivery can be planned at <36 weeks of gestation. Vaginal delivery is preferred. Cesarean delivery is reserved for obstetric indications.
Postpartum Care				
AFLP usually resolves completely after delivery with the return of normal liver function test within 7-10 days. Supportive prolonged care may be needed in cases of multiorgan dysfunction in form of mechanical ventilation, hemodialysis, nutritional support, and blood products transfusion.	MgSO4 is coming continued post-delivery. Blood pressure monitoring should continue at least 72 hrs of delivery and if possible by 7-10 days	MgSO4 is continued post-delivery. Platelet count usually decreases by 40 percent/ day, hematocrit falls, and liver enzymes increase in the first 48 hrs after delivery. Laboratory testing is advised 12 hourly in these patients.[3] If the platelet count continues to fall and LDH continues to rise after the fourth postpartum day,		-Pruritus disappears in the first few days of delivery with normalization of serum bile acids concentrations and other liver function tests.

		then diagnoses other than HELLP syndrome (eg, primary thrombotic microangiopathy) should be considered. However, these parameters may take longer to recover in cases of disseminated intravascular coagulation (DIC), platelet count less than 20,000 cells/microL, renal dysfunction, or ascites. Intensive monitoring may be needed in threatened or actual liver rupture or fulminant liver failure, DIC, acute kidney injury, massive transfusion, transfusion-related acute lung injury, and cardiac ischemia or cardiomyopathy.		
Perinatal and Long Term Outcomes				
Increased perinatal mortality and morbidity. Infants with LCHAD deficiency may have mild to severe long-term symptoms of neuropathy and retinopathy.	Growth restriction. Oligohydramnios. Preterm births. Low birth weight.	Perinatal mortality rate is 7 to 20 %. Preterm delivery. Growth restriction. No effect on fetal/neonatal liver functions but neonate may have leukopenia, neutropenia, and thrombocytopenia.	Reduced insulin sensitivity in pre-pubertal children.	Sudden intrauterine demise. Meconium staining of amniotic fluid. Preterm delivery. Neonatal respiratory distress syndrome.

Suggested Readings

1. Ellington SR, Flowers L, Legardy-Williams JK, Jamieson DJ, Kourtis AP. Recent trends in hepatic diseases during pregnancy in the United States, 2002-2010. Am J Obstet Gynecol. 2015 Apr;212(4):524.e1-7.
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DIC in Pregnancy

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Disseminated intravascular coagulation (DIC) during pregnancy is one of the leading causes of maternal mortality worldwide. Its rate varies from 0.03% to 0.35%. It is often secondary to underlying maternal and/or fetal complications. DIC is characterized by a concomitant over-activation of the coagulation and fibrinolytic systems, leading to widespread microvascular thrombosis, disruption of blood supply to different organs, ischemia, and multi-organ failure. This extensive activation of the coagulation cascade leads to consumption and depletion of platelets and coagulation proteins, which can provoke concurrent severe bleeding. Obstetric DIC more typically presents with bleeding, rather than thrombotic complications.

Physiology of Haemostasis

Normal haemostasis involves an interplay of regulation between coagulation and fibrinolysis. A fine balance is maintained between these two processes under normal circumstances to maintain blood in a fluid state. Coagulation is achieved by a cascade of enzymatic reactions, which involves a series of factors like zymogens-prekallikrein, prothrombin, and factors VII, IX, X, XI, and XII, which are converted to active proteases by hydrolysis. Two main pathways mediate blood coagulation, the intrinsic and the extrinsic pathways.

The intrinsic pathway is triggered when blood comes in contact with a foreign surface such as injured vessel endothelium. First platelets are activated and adhere to the site of injury. Then Prekallikrein is activated to kallikrein, which together with kininogen, sequentially activates factors XII, XI, and IX. The complex IX–X–VIII and Ca^{2+} activate factor X to Xa. This takes about 2-6minutes and is measured by APTT (activated partial thromboplastin time)

The extrinsic pathway is activated when blood comes in contact with damaged tissue. This generates factor Xa, by activating factor VII, Ca^{2+} and the thromboplastin (III) complex. This a faster process and takes only about 15sec and is measured by PT (prothrombin time).

Both the intrinsic and extrinsic pathways converge in the formation of factor Xa. The stages that follow are common to both pathways. Factor Xa converts prothrombin into thrombin. This reaction is accelerated by factor Va. Thrombin converts fibrinogen into fibrin. Finally, the fibrin monomers polymerize and trap the blood cells, generating the stable clot. (Figure 1)

Regulation of coagulation is achieved by removal of the factors involved in blood clotting, or by inactivating them. The α-thrombin–thrombomodulin complex activates plasma protein C, which degrades factors Va and VIIIa. Antithrombin III, a protease inhibitor, inactivates thrombin, kallikrein, IXa, Xa, XIa, and XIIa. Antithrombin III action is potentiated by heparin.

Fibrinolysis is the process that leads to clot dissolution. It is caused by hydrolysis of fibrin. This reaction is catalyzed by plasmin, which is generated from plasminogen. Conversion factor for plasminogen to plasmin includes factors XI and XII (intrinsic factors) and plasminogen tissue activator (extrinsic factor). There are inhibitors of fibrinolysis also present in form of plasminogen Activator inhibitor 1(PAI 1).

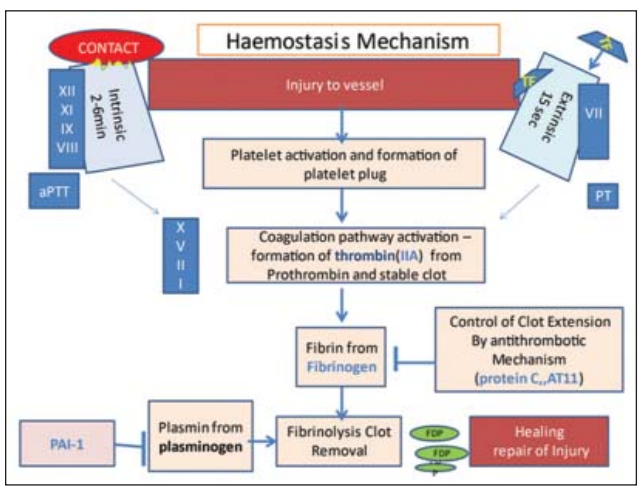

Fig 1: Normal mechanism of hemostasis

Pathophysiology of DIC

The Scientific and Standardization Committee (SSC) on DIC of the International Society on Thrombosis and Haemostasis (ISTH)[2] defined DIC as:

"An acquired syndrome characterized by the intravascular activation of coagulation with a loss of localization arising from different causes.

It can originate from and cause damage to the microvasculature, which if sufficiently severe, can produce organ dysfunction. Widespread clotting depletes the platelets and clotting factors that are needed to control bleeding and excessive bleeding occurs."

This definition highlights three important aspects:

1. DIC is always secondary to other causes, one of them being an obstetric cause , such as placental abruption, preeclampsia, or intrauterine fetal death.
2. DIC represents systemic pathological activation of coagulation. Normal haemostasis refers to the formation of a thrombus in response to endothelial damage and, in these cases, the clotting and fibrinolytic processes are limited to the site of endothelial injury. However, in DIC, there is uncontrolled dissemination of this localised thrombotic process which is clearly pathological. In obstetrical DIC, there is extraplacental dissemination of the activated coagulation system which is usually localised to the placenta.This wide spread thrombosis will activate excessive fibrinolysis and deplete coagulation factors leading to bleeding
3. The third crucial aspect is the role of microvasculature or the vascular endothelium which is the site of origin of DIC. Excessive and dysregulated thrombin generation due to (and causing) marked endothelial dysfunction can result in organ damage from microthrombi. If microvascular dysfunction led to organ damage, it would be considered DIC according to the ISTH definition

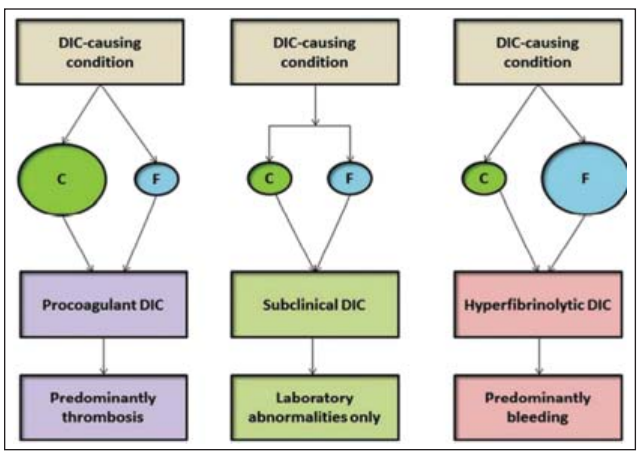

Fig 2: Conditions causing DIC

Since DIC is secondary to an underlying disease, the primary disease features may represent the clinical presentation of DIC. The type of DIC which will occur depends on pace and amount of thrombin generation. When there is a very rapid burst of large amount of thrombin ,it leads to rapid fibrinolysis and depletion of coagulation factors leading to haemorrhage such as in placental abruption, while slower release of excessive thrombin will result in thrombotic type of DIC such as in severe sepsis. Release of smaller amount of thrombin at a slow pace will be compensated by fibrinolysis simultaneously and DIC will remain sub clinical with only subtle changes in laboratory parameters such as in sepsis or fetal death. (Figure 2)

Pathophysiology of DIC in Pregnancy

Pregnancy is associated with adaptive changes in the coagulation system that are aimed to address the challenges posed by the need to have extra circulatory maternal blood flow through the placental bed. Thus, the mother has to protect herself from a life-threatening bleeding especially during labor and delivery on one hand, and secure a continuous blood flow through the placental bed to nourish the developing fetus on the other hand. The adaptive changes in the maternal hemostatic system are:

1. Excessive thrombin generation

   The excessive thrombin generation observed during normal pregnancy is supported by the observations of elevation in circulating maternal fibrinopeptide A, prothrombin fragments (PF) 1 and 2, and thrombin–antithrombin (TAT) III complexes during pregnancy especially at the time of and after normal labor and delivery. Subsequently in the course of the puerperium their concentrations decrease.
2. Increased agonist derived platelet aggregation
3. Two to three fold increase in fibrinogen concentrations
4. 20% to 1000% increase in factors VII, VIII, IX, X, and XII near term
5. 400% increase in von Willebrand factor
6. Decrease in Factors XIII and XI concentrations
7. No change in Factors II & V.
8. Decline in free protein S plasma concentration reaching a nadir at birth leading to an increase in resistance to activated protein C
9. Increase in concentration of PAI-1 (plasminogen activation inhibitor) by 3 to 4-fold during pregnancy and normal placental production of PAI-2 during normal pregnancy leading to reduction in fibrinolytic activity

Overall pregnancy is associated with increased clotting potential, as well as decreased anticoagulant properties and fibrinolysis.

During pregnancy there is increased risk of developing DIC as a result of different complications of pregnancy such as placental abruption, HELLP syndrome, preeclampsia, retained stillbirth, sepsis, post-partum hemorrhage (PPH), acute fatty liver, and amniotic fluid embolism. The most frequent pregnancy complication associated with pregnancy is placental abruption followed by PPH and preeclampsia. D-dimers and fibrin-degradation products that result from fibrinolysis interfere with platelet activation and can impair myometrial contractility and can contribute to PPH

It is important to understand the underlying mechanisms associated with the development of DIC in each complication as it will assist the clinician in the prevention and management of DIC in these cases.

Sepsis

Normal pregnancy is associated with activation of maternal leukocytes into a state akin to sepsis. Nevertheless, placental trophoblasts maintain a balanced systemic maternal inflammation during gestation by inactivation of maternal leukocytes. However, infectious agents like in septic abortion perturb this balance and can lead to the development of maternal DIC.

During sepsis the coagulation system can be activated by endothelial cells or leucocytes , platelets, and remnants of cell surfaces. These cells release proinflammatory cytokines such as tumor necrosis factor-α, interleukin-1 (IL-1) and interleukin-6 (IL-6), along with propagation of tissue factor (TF) expression on the surface of endothelial cells and leukocytes that can initiate an uncontrolled activation of the coagulation cascade via the TF/factor VIIa pathway leading to thrombin generation. If this coagulation response is uncontrolled it will eventually lead to DIC. Despite the potency of TF as a trigger of coagulation, potent anticoagulation pathways can control and limit its activity. However, all the natural anticoagulant pathways (ie, anti-thrombin III, protein C system, and TF pathway inhibitor [TFPI]) are compromised during sepsis mediated DIC. There is a continuous elevation of plasminogen activator inhibitor-1 (PAI-1) that suppresses fibrinolysis. Therefore sepsis produces a thrombogenic DIC with organ dysfunction. (Figure 3)

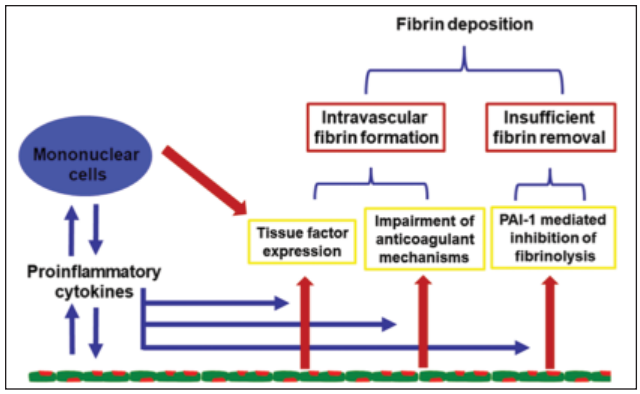

Fig 3: Mechanism of DIC in sepsis

Amniotic Fluid Embolism (AFE)

AFE is a major cause for maternal DIC, through a combined mechanism of activation of coagulation by the TF rich amniotic fluid debris that enters the maternal circulation and the acute systemic maternal inflammatory response which further propagates the activation of the coagulation cascade. These patients have a fibrinolytic type of DIC with bleeding.

Abruption

Patients who develop placental abruption suffer from a combined coagulopathy incorporating consumption coagulopathy and substantial release of thromboplastin (tissue factor) into the maternal circulation. In addition, local hypoxia and hypovolemia trigger endothelial response leading to increased expression of vascular endothelial growth factor, which causes an increased endothelial expression of TF.

Pre-eclampsia & HELLP

Endothelial damage, platelet activation and liver dysfunction occurs in PE, HELLP syndrome which can cause DIC. Recent advances in the understanding of the mechanisms of DIC in HELLP syndrome suggest that abruption rather than liver dysfunction is responsible for DIC. Rate of placental abruption was 5.6% in women with HELLP syndrome without DIC in comparison to 42.9% among those with DIC.

IUFD

There is slow release of thromboplastin from dead fetus leading to compensated DIC without any clinical manifestation mostly.

Acute Fatty Liver of Pregnancy

There is fatty microvesicular infiltration of hepatocytes. There is release of tissue factor from

damaged hepatocytes. The synthetic function of the liver is also hampered leading to lower production of fibrinogen and coagulation. Therefore compared to other forms of DIC longer time period is required for normalisation of level of coagulation factors.

Obstetric Haemorrhage

Rapid maternal loss of a large blood volume along with its coagulation factors leads to DIC with haemodynamic instability. At time of delivery there is procoagulant state and increased thrombin generation attributed to the release of TF into the maternal circulation following the separation of the membranes and the placenta; along with the systemic inflammation which accompanies the process of labor and delivery. The woman who have PPH have higher activation of coagulation cascade, beyond physiologic levels for normal pregnancy.

COVID-19 Infection

There is a combination of the systemic inflammatory response syndrome, disseminated intravascular coagulation and thrombotic microangiopathy in COVID 19 associated DIC.

Clinical Features

Typical hemorrhagic features of DIC include continued bleeding from venipuncture sites or indwelling catheters, generalized ecchymoses that develop spontaneously or with minimal trauma, bleeding from mucous membranes, unexpected and major bleeding from around drain sites or tracheostomies, and concealed hemorrhage in serous cavities (e.g., retroperitoneal hemorrhage). Bleeding in hemorrhagic DIC can be secondary to various reasons, including thrombocytopenia, platelet dysfunction, endothelial damage, interference of the fibrin degradation products with the clot structure, and rarely, consumption of clotting factors including fibrinogen to less than hemostatic levels. These considerations have obvious implications for planning treatments.

Typical thrombotic features of DIC are thrombophlebitis developing at unusual sites; respiratory distress syndrome; renal impairment without obvious explanations; central nervous system disturbances such as confusion and seizures (typically fluctuating in nature) ; dermal infarcts; skin necrosis; and greyish discoloration of finger tips, toes, or ear lobes (seen in extreme cases). Although macrovascular thrombosis may develop in DIC, it is usually not a presenting sign. In addition, sudden onset of hemorrhage is also quite uncharacteristic of patients with DIC and should persuade to look for other causes.

Diagnosis of DIC in Pregnancy

Diagnosis of DIC is made by clinical features depending on which phenotype is predominant and derangement of laboratory tests from normal values. (Table 1)

Table 1: Common Laboratory Tests for DIC

Test	Value
Platelet count	↓
PT	↑
INR	↑
APTT	↑
Fibrinogen	↓
D Dimers & FDP	↑

The hallmark of successful management of DIC depends on prompt diagnosis and accurate recognition. Using above criteria, diagnosis is made relatively late in the course of the disease. During pregnancy, there is a physiologic change in the maternal plasma concentrations of many of the coagulation parameters (Table 2) leading to a false perception that the status of the coagulation system is normal in cases when the patient is already developing coagulopathy. Moreover, often there is underestimation of the amount of bleeding and the relevant laboratory tests are performed too late when the patient is already compromised.

Table 2: Pregnancy Specific values of coagulation parameters

Non pregnant	Test	Trimester		
		1st	2nd	3rd
11-15	PT (Seconds)	9.7-13.5	9.5-13.4	9.6-12.9
0.9-1.3	INR	0.86-1.08	0.83-1.02	0.80-1.09
25-40	A PTT (Seconds)	23.0-38.9	22.9-38.1	22.6-350
	Fibrinogen (mg/dL)	244-510	291-538	301-696
	Platelet count (10^9/L)	174 to 391	155-409	146-429
	D dimers (micro gm/ml)	0.05-0.95	0.32-1.29	0.13-1.7

There is no single laboratory or clinical test that is

sensitive and specific enough to diagnose DIC and the risk to develop DIC is not evident in all cases. DIC is a dynamic situation that requires a continuous assessment of the clinical and laboratory parameters include decreasing concentration of fibrinogen and platelet count, prolongation of prothrombin time and increased concentration of fibrin split products or d-dimer. Taking this into consideration ISTH developed DIC scores (Table 3) taking change in PT value from control rather than absolute value, platelet counts ,fibrinogen and FDP level giving value 0-3 .A cumulative score above 5 is taken as overt DIC but this score does not take into consideration the physiological changes in pregnancy.

Pregnancy specific scores have been developed by various researchers. Of all these the most specific and sensitive is score developed by Erez et al (Table 4) This score gives more importance to fibrinogen and less to platelet count which can be decreased due to various reasons in pregnancy–unrelated to DIC. D dimers are not taken in consideration as they are increased in normal pregnancy as well and there is no upper limit. PT value increase from control value is used as cut off, keeping in mind the procoagulant state in pregnancy. The diagnostic performance of this score for DIC at a cutoff of ≥26 points was: 88% sensitivity, 96% specificity, a positive likelihood ratio (LR) of 22, and a negative LR of 0.125.

The incorporation of pregnancy specific scoring system to diagnose DIC in pregnant women is accurate, easy to use and may assist clinicians in real time in the Labor and Delivery wards. **But it is important that this assessment has to be repeated and the trend of change is more important than absolute values.** However, there is a need for an international consensus on the diagnostic criteria and scoring for DIC in pregnancy, this will facilitate standardization of the definition and will support international research effort in this dire complication of pregnancy.

Sepsis Induced Coagulopathy (SIC)

Sepsis is an important cause of DIC in pregnancy Recently, active members of the ISTH DIC-SSC proposed a simpler version for the diagnosis of SIC that is composed of only three items:

1. sepsis- definitions (infection with organ dysfunction),
2. platelet count
3. prothrombin time ratio

Table 5: SIC Score

Parameter	Score	ISTH	SIC
Platelet 10^9/L	2	<50	<100
	1	≥ 50 - <100	≥ 100 < 150
PT ↑ (difference in sec)	2	≥ 6	> 1.4
	1	≥ 3 < 6	≤ 1.2 <1.4
Fibrinogen	1	< 100 mg/dl	-
Sofa Score	2	-	≥ 2
	1		1

SIC score >=4 means patient is in DIC. (Table 5) A sequential diagnosis using SIC and overt DIC diagnostic criteria for every sepsis patient may be used. This strategy enables the early initiation of treatment without missing any therapeutic opportunities. Beneficial effects of anticoagulant therapy were observed in patients with coagulopathy as defined using both sets of criteria, suggesting that some patients who do not meet the criteria for overt DIC may benefit from anticoagulant therapy. Thus, the SIC diagnostic criteria may be valuable for detecting sepsis patients who are candidates for anticoagulant therapy

Table 3: ISTH DIC score

	Platelet 10^9/L			PT (↑ in Sec)			Fibrinogen mg/dL		FDP ↑		
	>100	<100	<50	<3	3-6	≥ 6	>100	<100	No	Mod	Strong
Score	0	2	3	0	1	2	0	1	0	2	3
>5	Overt										
<5	Non Overt										

Table 4: Pregnancy Specific DIC Score (Erez et al)

	Platelet 10^9/L				PT (↑ in Sec)				Fibrinogen mg/dL			
	>185	100-185	50-100	<50	<0.5	<0.5-1.0	1.0-1.5	>1.5	300	300-400	400-450	>450
Score	0	1	2	1	0	5	12	25	25	6	1	0
>26	Strong suspicion of DIC											

Point of Care Viscoelastic Tests

Thromboelastography (TEG); and Rotational Thromboelastometry (ROTEM) are the most widely studied viscoelastic tests which provide a rapid assessment of in vivo coagulation. Specific TEG/ ROTEM values were defined for pregnancy and at the time of delivery.

Treatment of DIC in Pregnancy

The basic principles for treating overt obstetric DIC are

1. Treatment and resolution of the underlying condition leading to DIC
2. Fast and prompt delivery or termination of pregnancy (before the threshold of viability). The delivery options should be discussed by a multidisciplinary team and consider the safest mode of delivery to the mother, how fast she is expected to deliver, what are the resources of blood products and other supportive mechanisms available, and can she sustain a surgery;
3. Supportive treatment with blood product transfusion, surgical care and related measures (Table 6)
4. Rigorous clinical and laboratory surveillance
5. Prompt involvement of needed consultant such as hematologists, gynecological surgeons, anesthesiologists
6. Timely referral to larger institute if facility for blood component replacement not available

Table 6: Blood component replacement

Component	Trigger	Increase
RBC	<7gm%	1 pack = 1 gm%
FFP	PT>1.5X	10-15m/kg = 30% ↑
Platelet	< 50000/dl	1 pack = 4000/dl
Cryo Precipitate	Fibrinogen <200 mg/dl	1 pool of 5 unit = 10 mg/kg
Fibrinogen Concentrate	Fibrinogen <200 mg/dl	60mg/kg = 100mg/dl

Treatment algorithms for haemorrhagic obstetric DIC always involve simultaneous blood product transfusion as a replacement of women's blood loss. During DIC there is a rapid consumption of fibrinogen and coagulation factors, making the monitoring and maintenance of proper blood products administration by conventional laboratory tests challenging, as rapid correction of blood component deficiencies is required at a rate faster than their depletion. Point of care tests like ROTEM\ TEG allow early detection and dynamic monitoring of clotting abnormalities, and transfusion needed; hence, they could potentially be used as guidance for administration of blood components.

Antifibrinolytic Agents

Tranexamic acid (TXA) has been suggested as a treatment for coagulopathy in PPH. TXA prevents the activation of plasminogen by plasmin by blocking its lysine binding sites. Four recent systematic reviews of the use of TXA for reduction of blood loss in PPH came to conflicting results. It can not help if coagulation factors are deficient so can be given only after replacing blood components. The usual dose is 1gm administered intravenously over 10 minutes up to 4 times daily.Patients with the organ failure or nonsymptomatic type of DIC may not benefit from antifibrinolytic agents as fibrinolysis is needed for the resolution of widespread fibrin thromboses resulting by DIC.

Recombinant Activated Factor VII (rFVIIa)

Administration of rFVIIa is warranted in active obstetrical hemorrhage that does not resolve by conventional treatment or to prevent hysterectomy. In such cases, this hemostatic agent decreases maternal mortality due to obstetrical hemorrhage.

However, as the use of rFVIIa increases the risk for arterial thrombosis by two fold, adequate thromboprophylaxis should be administrated to these patients following the acute hemorrhagic event. The optimal dose is unclear, however it is preferable to start with a low dose (40–60mcg/kg) to reduce the risk of thrombotic events

Fibrinogen Concentrate

Human fibrinogen concentrates have been used for substitution therapy in cases of hypofibrinogenemia, dysfibrinogenemia, and afibrinogenemia. It has the potential to administer relatively high quantities of fibrinogen in relatively low volume of transfusion in women with obstetrical hemorrhage. Its benefits are that it is readily available, as it can be kept in room temperature or refrigerators. Women with active obstetrical hemorrhage who have fibrinogen concentrations <200mg/dl can be given fibrinogen concentrate. However, it should not be given without finding value of fibrinogen. It is not widely available. Each vial contain 1000mg fibrinogen.

Recombinant Human Soluble Thrombomodulin (rhTM)

rhTM was reported to potentially lower morbidity and mortality of patients with DIC due to sepsis.It reduces excessive thrombin activation and regulates the imbalance of the coagulation system. There is a need for more substantial evidence prior for the inclusion of rhTM in the treatment protocols for obstetrical DIC.

Anticoagulants

In cases of DIC with predominant hypercoagulation and thrombotic phenotype heparin can be used to partly inhibit coagulation. Low molecular weight heparin (LMWH) is superior to unfractionated heparin (UFH) for treating this type of DIC. However, the majority of cases of DIC in pregnancy are associated with a hemorrhagic phenotype of DIC, and heparin may increase bleeding, especially if adequate replacement therapy for consumed clotting factors has not been achieved, hence it is not recommended.

Management of Non Overt DIC

Since DIC is always a secondary phenomenon, a DIC screen should always be done when risk factors for DIC are present and it should be repeated till the risk factor is taken care of. The frequency of testing will depend on the underlying cause.Using the DIC score will enable early diagnosis of DIC

Conclusion

DIC in obstetrics is a life-threatening complication that is secondary to obstetrical and non-obstetrical related complications of pregnancy. The diagnosis of DIC can be elusive during pregnancy and requires vigilance and knowledge of the physiologic changes during pregnancy. Detection at subclinical phase by keeping high index of suspicion of DIC in conditions which predispose to DIC and utilising pregnancy specific scores can help detect subclinical DIC. Removal of the trigger for DIC is most important. Point of care testing can facilitate the diagnosis and the management of DIC in pregnancy.

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Dyspnea in Pregnancy: How to Approach?

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Introduction

Dyspnea is defined as a "subjective experience of breathing discomfort that is comprised of qualitatively distinct sensations that vary in intensity". Patients often present with this complaint in pregnancy and need proper evaluation to assess its severity. Pregnancy induced changes occuring in maternal respiratory system cause physiological dyspnea. On the other hand complications developing in cardiopulmonary system in pregnancy cause pathological dyspnea necessitating intensive management. In this article we focus on the characteristics of physiological dyspnea, its differentiation from other pathological causes of dyspnea and recognition of acute respiratory failure along with its initial management.

Etiology of Dyspnea in Pregnancy

There are several causes of dyspnea in pregnancy. They can be divided into pulmonary, cardiac, neurologic, metabolic, miscellaneous and causes specific to pregnancy. The causes are shown in Table 1.

Changes in Respiratory System in Pregnancy

Physiological dyspnea is a commonly seen condition in pregnancy (60% in women on exertion and 20% at rest) and occurs due to the following reasons-

- Anatomical changes: The enlarged uterus causes a 4.0 cm maximal increase in the level of the diaphragm, together with a 2.1 cm maximal increase in the transverse diameter of the chest. The subcostal angle increases progressively from an average of 68.5° in early pregnancy to 103.5° in late pregnancy, which remains the maximal inspiratory and expiratory pressure, and compensates for the reduction in abdominal replacement.
- Hormonal changes: Progesterone acts as trigger for the primary respiratory centre by lowering the threshold and increasing the sensitivity of the respiratory centre to CO2, while estrogen increases the number and sensitivity of progesterone receptors in the hypothalamus and medulla (central neuronal respiratory centres). *Under the effect of progesterone, depth of respiration increases; rate however remains constant; Tidal volume increases by 40%; the minute volume (respiratory rate multiplied by tidal volume) increases by 40%, from 7.5 L/min to 10.5 L/min; the increase in ventilation is greater than the corresponding elevation in oxygen consumption (approximately 20 percent).*

Table 1: Causes of dyspnea in pregnancy

Pulmonary	Cardiac	Neurologic	Metabolic	Miscellaneous	Specific to pregnancy
COPD exacerbation	RHD	Stroke	Sepsis	Hyperventilaton	Preeclampsia
Asthma exacerbation	Cardiomyopathy	Neuromuscular disease	Diabetic ketoacidosis	Anxiety	Eclampsia
COVID-19 infection, H1N1 virus infection, Pneumonia	High output failure		Severe anemia	Anaphylaxis	Peripartum cardiomyopathy
ARDS secondary to MODS	Cardiac tamponade		Salicylate, CO or organophosphorous poisoning	Massive obesity	Amniotic fluid embolism
Pulmonary embolism	Arrhythmia			Ascites	Tocolytic induced pulmonary edema
Pneumothorax	Decompensated heart failure			Pleural effusion	Physiologic dyspnea
Pulmonary contusion	Acute coronary syndrome			Pneumo-mediastinum	

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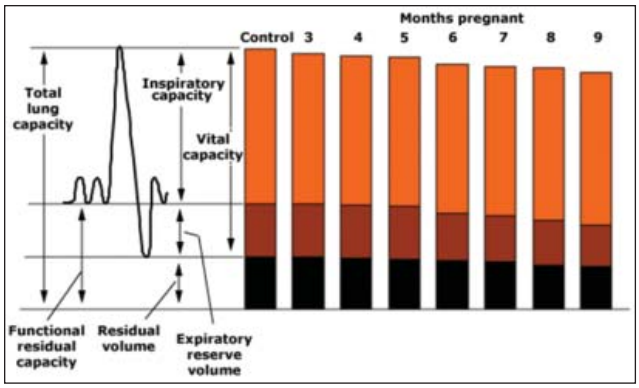

Fig 1: Changes in pulmonary function test in pregnancy

On serial measurements of lung volume compartments during pregnancy, functional residual capacity decreases approximately 20% during the later half of pregnancy, due to a decrease in both expiratory reserve volume and residual volume.

Physiological dyspnea can be differentiated from pathological dyspnea by the following:

- Physiological dyspnea begins from the end of 1st trimester/beginning of 2nd trimester and is gradual in onset.
- It is not associated with signs and symptoms like cough, chest pain, fever, hemoptysis, urticaria, wheezing, tachycardia or hypoxemia.
- It is not associated with abnormal findings on respiratory and cardiovascular examination such as crackles, rhonchi, whispering pectoriloquy, broncophony or murmurs on CVS examination.

Arterial Blood Gas Changes in Pregnancy

As a result of the progesterone-induced increase in alveolar ventilation, arterial PCO_2 falls to a plateau of 27 to 32 mmHg during pregnancy. This respiratory alkalosis is followed by compensatory renal excretion of bicarbonate so that the resultant arterial pH is normal to slightly alkalotic (usually between 7.40 and 7.45). The maternal arterial oxygen tension (PaO_2) is generally increased because of hyperventilation, ranging from 106 to 108 mmHg in the first trimester to 101 to 104 mmHg in the third trimester.

Effects on Fetus Due to Dyspnea

Blood gas abnormalities in dyspnea can adversely affect the fetus. Studies have suggested that while excessive hypocapnia and hypoxemia in mother can lead to harm in fetus due to poor placental perfusion, maternal hypercapnia leads to respiratory acidosis in the fetus which do not have ominous effects on the fetus.[13] Evidence states that maternal hypocapnia causes lower Apgar score and delayed neonatal breathing, while hypercapnia in mother has resulted in statistically significant higher Apgar score at delivery. So, permissible hypercapnia with PaCO2 maintained <60mmHg has been recommended in pregnancy.

Low birth weight babies and preterm deliveries in women with dyspnea have been found, but inadequate evidence still looms large to comment specifically on this correlation.

Severity of dyspnea: It can be assessed by the Modified Medical Research Council (mMRC) dyspnea scale or The Modified Borg Scale, Table 2 & 3.

Table 2: Modified Medical Research Council (mMRC) dyspnea scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise.
1	I get short of breath when hurrying on level ground or walking up a slight hill.
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace.
3	I stop for breath after walking about 100 yards or after a few minutes on level ground.
4	I am too breathless to leave the house or I am breathless when dressing.

Table 3: The Modified Borg Scale

0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight (light)
3	Moderate
4	Somewhat severe
5	Severe (heavy)
6	
7	Very severe
8	
9	
10	Very, very severe (maximal)

*Score 6, 8 & 9 are not assigned any severity

Acute Respiratory Failure in Pregnancy

Acute respiratory failure is a rare but life threatening cause of dyspnea in pregnancy, requiring mechanical ventilation. It may occur in 0.1-0.2 % of all pregnancies. Acute dyspnea is the development of symptoms over hours to days whereas chronic

dyspnea is presence of symptoms for last 4-8 weeks, usually secondary to some underlying disorder in the pregnant woman.

Recognition of Acute Respiratory Failure

1. Rapid shallow breathing- RR > 25/min; as discussed above, the physiological changes of pregnancy results in increased tidal volume which increases the depth of respiration. However the rate remains same. An increase in respiratory rate is an important sign of maternal deterioration.
2. Heart rate >120 beats/min
3. Use of accessory muscles of respiration and flaring alae nasi
4. Confusion, agitation, somnolence which may be due to brain hypoxia
5. On auscultation of chest- Crackles, wheeze, whispering- pectoriloquy, bronchophony
6. On pulse oximetry a low spo2 < 90% is a sign of respiratory failure
7. On ABG partial pressure of oxygen (pao2) < 60 mm Hg
8. Diaphoresis, substernal pain, cyanosis or hemoptysis.

Approach to Diagnosis of Acute Dyspnea in Pregnancy

When a pregnant woman reports dyspnea, the clinician should be able to differentiate a new onset acute disorder (like COVID-19 infection), an exacerbation of any underlying disorder (like asthma) or physiological dyspnea.

Management of Acute Respiratory Failure

Initial management of all cases with respiratory failure is same with the aim to stabilize the patient. Once the patient is stabilized is the definite management instituted according to the diagnosis.

Table 4: Differential diagnosis of common causes of dyspnea in pregnancy

Disease	History, Symptoms & Signs	Lab Investigations
Physiological dyspnea	No associated wheeze, cough, chest pain	Normal
COVID-19 infection	H/o contact with COVID-19 positive person, H/o travel, fever, sore throat, cough, myalgia.	Leucopenia, thrombocytopenia, increased D-dimer, CRP, Ferritin, SARS CoV-2 RTPCR positivity, CXR: ground glass opacity
Asthma exacerbation	H/o similar attacks before pregnancy, subacute/chronic cough, dyspnea, wheezing	Evidence of reversible airflow obstruction on pulmonary function tests,[17] response to bronchodilators
Pulmonary edema	H/o underlying heart disease, severe pre eclampsia, eclampsia, Cough, nocturnal dyspnea, orthopnea, gallop rhythm, crackles on auscultation	CXR: cardiomegaly,interstitial edema Echo: Left ventricular dilatation, evidence of valvular disease, NTProBNP levels>50pg/ml
Pulmonary embolism	Sudden onset dyspnea/wheezing, tachypnea, pleuritic chest pain	Arterial hypoxemia, Duplex USG to rule out DVT, V/Q scan or CTPA to detect abnormal perfusion
Peripartum cardiomyopathy	H/o gradual onset dyspnea after 36 weeks gestation, cough, orthopnea, tachycardia, jugular venous distension, arrythmia, rales on auscultation	Echo: Ejection fraction <45%, ventricular dilatation and dysfunction, CXR: enlarged cardiac silhouette
Amniotic fluid embolism	Sudden onset dyspnea during labour/ delivery, shock, cyanosis, cardiac arrest	Disseminated intravascular coagulation, evidence of fetal elements in maternal lungs
Acute upper airway obstruction	H/o exposure to allergens or foreign body aspiration, tachycardia, wheezing, urticaria, itching	Diagnostic endoscopy in case of foreign body aspiration, pulmonary function tests showing disproportionate reduction of peak expiratory flow, response to bronchodilators in case of exposure to allergens
TRALI	H/o transfusion of plasma containing blood products within 6 hours, sudden onset dyspnea, wheezing, hematuria	CXR: bilateral pulmonary infiltrates, evidence of hypoxemia

The steps of initial management are

Oxygenate the patient – The goal is to achieve a saturation of >95% which translates to a PO2 > 70 mm Hg. The preferred method of administering the oxygen depends upon the severity of the hypoxemia. For patients with mild hypoxemia, administration via nasal cannula may be sufficient. More severe hypoxemia generally requires administration via a facemask, high flow nasal cannula, or a non-rebreather mask.

The important features of different devices which are used to deliver oxygen are:

Prongs- nasal prongs are used when the requirement of oxygen is from 1L/min to 6 L/ min (Fig 2). They are used to deliver a FiO_2 (fraction of inspired oxygen) of 0.24 to 0.44. If requirement is more than 6 L/min they will not be useful and the above goal is not met a face mask should be used.

Face mask (Fig 3)- A simple face mask can deliver a FiO_2 of upto 0.6 and is used with oxygen flow rate of 5L/min to 8L/min . So if requirement is more than 8 L/min, we should use the next device

Oxygen mask with reservoir bag (Fig 4)- If requirement of oxygen is more than 8 L/min, the mask with reservoir bag should be used. These are of 2 types- partial re-breathing mask (8-12 L/min, delivers FiO_2 of 0.5-0.7) and nonrebreathing mask (10-15 L/min, delivers FiO_2 of 0.7-0.9). These masks are very useful for short term oxygenation when high FiO_2 is required. Any patient who needs a high FiO_2 of more than 0.6 for many hours should receive positive pressure ventilation

Ventilation: If the patient is not oxygenated with the above measures she will need positive pressure ventilation, which may be either non-invasive ventilation or invasive ventilation over endotracheal intubation. Noninvasive ventilation has the advantage that it avoids intubation. However due to the raised intragastric pressure during pregnancy and decreased stomach emptying time, these patients are more prone to aspiration. On the other hand intubation in pregnancy is also more difficult and challenging because of difficult airway. Failed intubation is 8 times more common in obstetric population than other adults.

The main indications for intubation are as follows:

- Not achieving oxygenation goals with prongs/ face mask.(PaO_2<60mmHg)
- Not getting ventilated- as indicated by high PCO_2 on ABG
- Circulatory collapse
- Altered mentation with GCS <8

Maternal positioning: Head end of bed elevated or left lateral positioning to avoid aortocaval compression

Hydration: secure good iv access for any fluid or injectable drugs. Input output monitoring to be strictly done hourly to avoid fluid overload, causing worsening of the situation.

Urgent investigations which are required for therapeutic and diagnostic decision are:

- In this era of COVID-19 pandemic, the first investigation to be done at contact is the Rapid Antigen Test for COVID-19 and isolate her accordingly, while taking her nasal and oropharyngeal swabs and awaiting SARS Co-V 2 RTPCR results
- ABG- identifies and quantitates the severity of any ventilatory abnormalities. it also guides ventilator adjustments in mechanically ventilated patients. It should be repeated every 4-6 hourly to avoid any marked respiratory alkalosis(because it may decrease uterine blood flow) or metabolic acidosis.
- A complete blood count- leuckocytosis can point towards sepsis/ ARDS and leucopenia can be a result of viraemia and also in severe sepsis. thrombocytosis may be an indication of

Fig 2: Nasal prongs

Fig 3: Simple face mask

Fig 4: Face mask with reservoir Bag

purulent collection in closed spaces (empyema, pyoperitoneum) whereas thrombocytopenia may be seen in sepsis and DIC.

- Baseline KFT, LFT, serum electrolytes to evaluate the organ functions and rule out ARDS secondary to MODS
- A urine routine and microscopy and culture is essential pyelonephritis is one of the common cause of sepsis and ARDS in pregnancy.
- Coagulation profile for monitoring patients with MODS, pulmonary embolism
- Serum TSH as hyperthyroidism or hypothyroidism can also present as dyspnea.
- X-ray chest to narrow the differential diagnosis and confirm placement of ET tube
- ECG to assess cardiac status
- Echo is a very important investigation in acute respiratory failure to determine the severity of ventricular dysfunction.
- POCUS (point of care USG)- lung ultrasound can help in diagnosing pneumothorax, pleural effusions, pulmonary edema and pulmonary consolidation. there are specific ultrasound patterns seen for a normal lung, a pneumothorax, interstitial edema, and pneumonia
- Other focused investigations according to suspected pathology which has been zeroed down by initial investigations, as mentioned in Table 4.

Specific treatment of patient according to the suspected or diagnosed pathology:

- Pulmonary edema: use of diuretics (frusemide), vasodilators (nitroglycerine, nitric oxide)
- Pulmonary embolism: Low molecular weight heparin 1mg/kg every 12 hours
- COVID-19 infection: Use of drugs like Azithromycin, Tocilizumab, monoclonal antibodies according to severity
- Exacerbation of asthma: Use of beta-2 agonists, systemic glucocorticoids and Ipratropium bromide.
- Community acquired pneumonia: Judicious administration of intravenous antibiotics.
- ARDS secondary to MODS: Correction of underlying disorder
- Severe anemia resulting in dyspnea is not an uncommon clinical scenario in our country. Investigating the type of anemia and its prompt management along with blood products transfusion is life saving.

Expedite delivery after stabilization of the patient especially if patient is near term.

- Studies have suggested that delivery of fetus helps in improving the maternal condition in ventilated patients, while others have stated that given the risks of inducing labour or performing a caesarean, the indications for delivery should be obstetric.[23,24]
- The mode of delivery should be guided by obstetric indications. Adequate pain relief should be given to labouring patients to decrease hyperventilation and hence marked respiratory alkalosis.
- Perimortem caesarean section is indicated in patients with cardiac arrest if return of spontaneous circulation does not occur within 4 minutes of effective cardiopulmonary resuscitation.
- Drugs like Carboprost and ergot alkaloids are not to be used for control of postpartum hemorrhage in such cases as they cause bronchoconstriction.
- Epidural analgesia is preferred for the asthmatic patient as it reduces oxygen consumption in the first and second stage of labour and can provide adequate anaesthesia if caesarean section is required. If general anaesthesia is required, ketamine and halogenated anaesthetics are pereferred as they have brochodilatory effect.

Conclusion

Dyspnea in pregnancy can be harmless if physiological, but can lead to grave conditions if underassessed and pathological. Hence as obstetricians, we should possess an optimum level of alertness to ascertain the severity of dyspnea in an apparently well pregnant woman to prevent its progression to fatality and thereby improve the overall feto-maternal outcome in such conditions in our settings.

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Management of Obstetric Shock

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Introduction

Shock is a state of reduced tissue perfusion that causes cellular hypoxia. It is a state of acute circulatory failure with inadequate or inappropriately distributed tissue perfusion.[1] The effect as well as the management strategy is different in pregnant women as the normal physiologic changes occur in the most organ systems during pregnancy, also the mother and the foetus are both vulnerable during pregnancy. There are various types of shock depending upon their respective pathophysiology but all have a final stage of multiorgan failure as a result of the imbalance between oxygen demand and supply. Haemorrhagic shock is the most common type encountered in pregnant population. The primary goal in management is to stabilise the women with restoring the cardiac function. In this chapter we will discuss about the causes, signs to identify and treatment of different type of obstetric shock.

Pathophysiology of Shock

When there is compromised end organ perfusion, there is switch from aerobic to anaerobic metabolism compensates temporarily. As a result of this anaerobic metabolism lactate accumulates in cells. Hypoxia eventually causes cellular and then tissue necrosis.[1,2]

Types of Shock

They are classified as follows:

- Hypovolemic shock
- Distributive shock
- Cardiogenic shock
- Obstructive shock

They require specific management owing to differences in their pathogenesis and pathophysiology.[2]

Hypovolemic Shock

Hypovolemic shock is a condition of inadequate organ perfusion caused by loss of intravascular volume. The important causes are

- Antepartum haemorrhage
- Postpartum haemorrhage
- Acute gastroenteritis

Distributive Shock

Distributive shock is a state of relative hypovolemia resulting from pathological redistribution of the absolute intravascular volume. The causes are

- Septic shock
- Anaphylactic shock

Cardiogenic Shock

Cardiogenic shock is primarily a disorder of cardiac function in the form of a critical reduction of the heart's pumping capacity, caused by systolic or diastolic dysfunction leading to a reduced ejection fraction or impaired ventricular filling. It is defined by systolic arterial pressure (SAP) <90 mmHg or mean arterial blood pressure (MAP) of 30 mmHg below the baseline value and cardiac index (CI) <1.8 L/min/m2 without pharmacologic or mechanical support or <2.0 L/min/m2 with support.[3] The causes are

- Rheumatic heart disease
- Pre-eclampsia
- Severe anemia
- Peripartum cardiomyopathy
- Amniotic fluid embolism

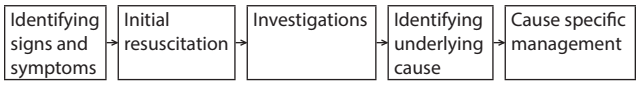
Obstructive Shock

Obstructive shock is a condition caused by the obstruction of the great vessels or the heart itself. The causes are

- Cardiac tamponade
- Pneumothorax
- Pulmonary embolism

How to Approach in a Case of Obstetric Shock

Whenever a pregnant woman presents in emergency with features of shock, clinical assessment for evaluating the underlying cause and management should be done simultaneously. It should be as follows:



Signs and Symptoms of Shock

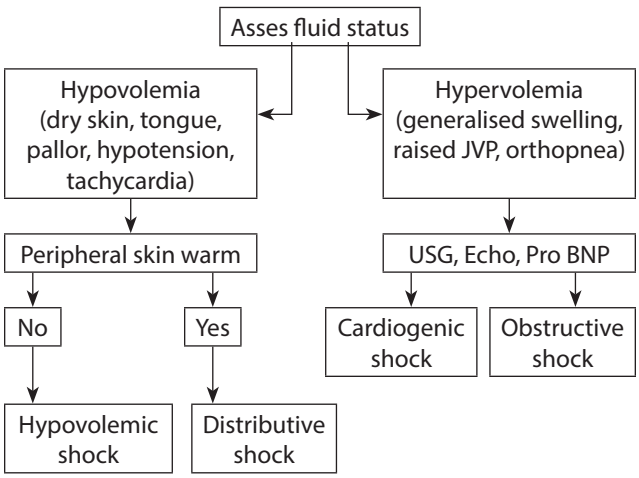
The woman present with an altered sensorium,

cold calmy periphery, tachycardia, tachypnoea, hypotension. There can be oliguria, desaturation depending on the intensity and duration of tissue hypoxia.

Initial resuscitation: It should follow the Basic Life Support (BLS) protocol. The aim of resuscitation is to prevent shock worsening and to restore the circulation to a level that meets the body's tissue oxygen requirements. Simultaneously arrangements for adequate fluid, blood and blood products have to be ensured. Any significant previous history or predisposing event must be enquired and documented properly from the accompanying relative.

Investigations: Whenever a patient comes to the emergency basic investigations must be done on priority basis along with resuscitation. Blood for grouping and crossmatching, complete blood count, liver function test, kidney function test, coagulation profile (when required), complete ABG with lactate level should be done.

After initial resuscitation the woman to be assessed as follows:



Specific treatment can be initiated after identifying the actual type of shock.

The two common types of shock identified in reproductive age groups are hypovolemic shock (most commonly due to haemorrhage) and septic shock. These will be discussed with details in this chapter.

Hypovolemic shock: As discussed earlier, hypovolemic shock occurs due to loss of intravascular volume that decreases the preload and cardiac output. In pregnant and postpartum women, the most common predisposing factor is blood loss. The symptoms are pallor, sweatiness or cold clammy skin, rapid breathing, anxiousness, confusion or unconsciousness and scanty urine. The signs are altered mentation (GCS<15), tachycardia (pulse rate >110 /min), capillary refilling time (CRT) >2 sec, low blood pressure (mean arterial pressure <65mmHg), shock index ≥ 1 tachypnoea (respiratory rate >30 breaths/min) and oliguria (urine output <30ml/h). The clinical signs also correlate with grade of blood loss and it is classified in Table 1.

Table 1: Grading of blood loss and presenting features

Parameters	Class 1	Class 2	Class 3	Class 4
Blood loss (%)	15%	15-30%	30-40%	>40%
Blood loss (ml)	<1000	1000	2000-2700	>2700
Respiratory rate (per min)	14-20	20-30	30-40	>40
Heart rate (per min)	<100	>100	>120	>140
Systolic BP	Normal	Normal	Decreased	Decreased
Diastolic BP	Normal	Increased	Decreased	Decreased
Mental status	Anxious	Anxious	Confused/ agitated	Lethargic
Urine output (ml/hr)	>30	20-30	5-15	negligible

Shock index: Shock index is heart rate divided by systolic blood pressure (HR/SBP). The normal value is 0.5-0.7, if it is more than 0.9-1.1, intensive resuscitation required.[4]

Also, the prognostication is done using MEOWS score (Modified early obstetric warning system). Carle's obstetric early warning score is described in Fig 1.[5]

	3	2	1	0	1	2	3
Systolic blood pressure (mmHg)	< 80	80–89		90–139	140–149	150–159	≥ 160
Diastolic blood pressure (mmHg)				< 90	90–99	100–109	≥ 110
Respiratory rate (min⁻¹)	< 10			10–17	18–24	25–29	≥ 30
Heart rate (min⁻¹)	< 60			60–110		111–149	≥ 150
% O_2 required to maintain SpO_2 ≥ 96%				Room air	24–39%		≥ 40%
Temperature (°C)	< 34.0		34.0–35.0	35.1–37.9	38.0–38.9		≥ 39
Conscious level				Alert*			Not alert†

Urine output, pain score, F_iO_2 and S_aO_2 recorded elsewhere on chart. Alert*, alert and orientated, equivalent to Glasgow Coma Score (GCS) 15 and A on Alert/Voice/Pain/Unresponsive (AVPU) scale; Not alert†, GCS 3–14 or V, P, U on AVPU scale.

Aggregate score: 0- routine care, 1-3- low grade response, 4-5- medium grade response, ≥6- high response

Fig 1: Carle's obstetric early warning score

Management: The management starts with initial resuscitation, then after determining the exact cause the specific treatment is initiated.

Immediate Management

- CALL FOR HELP
- Monitor vital signs
- Make sure that the airway is not obstructed
- Give oxygen at 6-8L per minute by mask or nasal cannula
- Tilt pregnant woman to the left side (15°-30°)
- Keep the woman surroundings warm and her warm
- Start an IV infusion (two, if possible) using a large-bore (16-gauge or largest available) cannula or needle
- Collect blood for estimation of hemoglobin, blood grouping, immediate cross-matching (coagulation profile and bedside clotting test in cases of hemorrhagic shock) just before infusion of fluids
- Rapidly infuse IV fluids (0.9% NS or Ringer's lactate) initially at a rate of 1 L in 15-20 minutes. Give fluid as bolus of 500ml
- Aim to replace two to three times the estimated blood loss. Give at least 2 L of these fluids in the first hour. Don't give more than 2.5 lit of fluid
- Replace the loss, arrange adequate blood and blood products
- Catheterize the bladder and monitor urine output and fluid intake

Specific Management

1. Hemorrhage
   - Take steps to stop bleeding (e.g., uterotonics, uterine massage, bimanual compression, aortic compression, and inform the Maternity OT and required staff to prepare for surgical intervention)
   - Transfuse blood products as soon as possible to replace blood loss in the ratio 1:1:1
   - Temporary measures to control bleeding like aortic compression
   - Determine the cause of bleeding and manage accordingly
2. Acute gastroenteritis
   - Fluid resuscitation
   - Antibiotics (if bacterial enteritis suspected)
   - Electrolyte correction

The signs of improvement are: Response to fluid should be reassessed within 30 minutes for signs of improvement

- Stabilizing pulse: rate of 90/min or less
- Increase in blood pressure: MAP 65 mmHg or more
- Improving shock index
- Improved mental status: less confusion or anxiety
- Increase in urine output: 30ml/hour or more
- Continue management of underlying cause
- Adjust fluid according to hydration status

Septic shock: The term sepsis and septic shock has been defined with help of clinical and laboratory criteria. It is linked with infection and inflammatory response, but the defining parameters have changed since times. The Sepsis-3 task force in 2016 has given the new definition of sepsis and septic shock.[6,7] Sepsis is now defined as 'life threatening organ dysfunction caused by dysregulated host response to infection'. It is diagnosed as presence of infection and a raised Sequential Organ Failure Score (SOFA), with a change of score of 2 or greater.[8] (table 2)

Role of Quick SOFA

SOFA is well known within the intensive care community, but not applied widely. It is complex, cumbersome and also the information required to calculate the score may not be available at the first point of contact when the patient is acutely ill. The task force developed a simple bedside tool to identify those with infection who are more likely to have poor outcomes, quick SOFA. (table 3)

Table 2: Sequential Organ Failure Assessment Score (SOFA) Score

SOFA score	0	1	2	3	4
Respiration PaO_2/FIO_2 or SaO_2/FIO_2 mmHg	>400	<400 221-301	<300 142-220	<200 67-141	<100 <67
Coagulation	>150	<150	<100	<50	<20
Liver Birilubin(mg/dl)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular Hypotension	No hypotension	MAP <70	Dopamine ≤5 or any	Dopamine >5 or notepinephrine ≤0.1	Dopamine >15 or norepinephrine >0.1
CNS (GCS)	15	13-14	10-12	6-9	<6
Renal Creatinine (mg/dl) or urine output (ml/d)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or <5.00	>5.0 or <200

Table 3: qSOFA score

q SOFA score		
Respiratory rate	>22/min	1 point
Mentation	Altered	1 point
Systolic blood pressure	< 100 mm of Hg	1 point

Septic shock is defined as a 'subset of sepsis with profound circulatory, cellular and metabolic abnormalities associated with a greater risk of mortality than sepsis alone'. It is diagnosed as sepsis with vasopressor requirement to maintain a MAP of >65 mmHg and serum lactate level >2 mmol/L.

WHO (2018) has defined maternal sepsis as 'a life threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post abortion or postpartum period'.[9]

The signs and symptoms are hyperthermia in early phase followed by hypothermia, altered mental status, tachycardia (heart rate > 100/min), tachypnea (respiratory rate > 22 breaths/minute), Mean Arterial Pressure (MAP) < 65mm Hg, requirement of vasopressors to maintain MAP ≥ 65 mm of Hg, oliguria or anuria. There may be clinical presentation related to the septic foci (vaginal discharge, uterine tenderness or SSI).

The prominent causes are chorioamnionitis, septic abortion- retained products of conception, invasive procedures (amniocentesis, chorionic villus sampling), post-partum endometritis, thrombophlebitis, surgical site infections, pyelonephritis, mastitis, pneumonia, necrotizing fasciitis, peritonitis or pelvic inflammatory disease.

Management: The optimum management of sepsis lies in early recognition and prompt initiation of resuscitation. The initial resuscitation and the investigation go hand in hand.

To assess end organ hypoperfusion	**To assess infective organism**
Complete blood counts, Kidney function tests, Liver function tests, Serum electrolytes, Arterial blood gases with lactates, Coagulation profile, Blood sugar	Blood culture, High vaginal swabs, Urine culture, Wound swab culture, Products of conception for culture, peritoneal fluid/pleural fluid culture if relevant

Early management comprises six management bundle to be completed within 1 hour which is also called **the one-hour bundle** or the **golden hour of sepsis**.

Anaphylactic shock: It is another type of distributive shock. Anaphylactic shock is caused by massive histamine-mediated vasodilation and maldistribution with a shift of fluid from the intravascular to the extravascular space. The clinical presentation varies according to the dose and site of entry of the antigen and the degree of sensitization. Initially, skin manifestations, abdominal symptoms, or respiratory symptoms may be prominent. Late reactions include arrhythmias, myocardial ischemia, and respiratory failure may manifest as late as 12 hours after the initial event. For treatment of anaphylactic shock especially the administration of Injection Adrenaline 0.5mg IM (1:1000) and forced fluid replacement are required. In patients with bronchospasm, β-sympathomimetics and, as second line treatment, glucocorticoids are indicated (as they are in patients with delayed progressive symptoms). Histamine antagonists suppress the histaminergic effects.[12]

Cardiogenic shock: Echocardiography and invasive monitoring are the pillars of diagnosis. The primary goal of treatment is removing the cardiac causes of the shock. Oxygenation, inotropic drugs, positive pressure ventilation, urgent cardiology consultation are the mainstay of treatment. Specific treatments are as per cardiology consultation.

Obstructive shock: Although the symptoms resemble those of cardiogenic shock, obstructive shock needs to be clearly distinguished from the latter because it is treated quite differently. Obstructive shock needs immediate cause specific treatment. Simple measures may suffice, such as changing the position of a patient with caval compression syndrome or adjusting the ventilation of the patient where the level of PEEP is too

ONE HOUR BUNDLE - Initial Resuscitation Goals

- Administer oxygen- the aim is to maintain SpO2 at >94%
- Measure lactate level- Initial lactate >2 mmol/L represents tissue hypoperfusion
- Blood Cultures- At least 2 sets (aerobic and anaerobic) ideally before starting antibiotics, or within 45 minutes of therapy
- Administer broad spectrum antibiotics – The empirical therapy should not be delayed for obtaining cultures. The drug of choice is piperacillin with tazobactum 4.5 gm 6 to 8 hourly or cefoperazone and sulbactum 3gm 12 hourly. In case of suspected MRSA add vancomycin 1gm 12 hourly or targocid 400mg 12 hourly for 3 doses followed by 400mg 24 hourly. (Dose should be modified according to creatinine clearance)
- Administer IV Fluids - Crystalloid 30 ml/kg (RL or NS) in boluses within 3 hours of recognition. Patient should be closely monitored after each bolus of fluid for her pulse, BP, respiratory rate, SpO2 and basal crepitations to see response and also to diagnose pulmonary edema. Further fluid should be given according to the fluid responsiveness of the patient. Colloids may be associated with increased risk of acute kidney injury.[10,11]
- Vasopressors- Should be commenced in 1st hour if MAP is not ≥ 65 mm Hg after fluid resuscitation. Norepinehrine is the first line vasopressor; vasopressin can be added if MAP target is not met. Dopamine is not the preferred drug for septic shock

high. According to the underlying cause of the obstruction, a pulmonary embolism is treated with thrombolysis; tension pneumothorax or pericardial tamponade are relieved immediately by thoracic or pericardial drainage.[13]

Conclusion

Shock is defined by critical tissue hypoperfusion. It must be rapidly reversed before irreversible organ damage occurs. Treatment should therefore begin in the ER with initial resuscitation and should consist of oxygen therapy with or without ventilatory support and a rapid appraisal of the likely causes. In hemorrhagic shock the cause is to be treated promptly. In all other shock states, except cardiogenic shock with left ventricular failure, intravenous fluids are indicated. Investigations should be sent accordingly. In fluid unresponsive women invasive haemodynamic monitoring and repeated IV fluid challenges with CVP guidance should be considered. In shock states unresponsive to intravascular fluid expansion, or in cardiogenic shock where fluid challenges may be hazardous, inotrope therapy is required. The choice of inotrope should be guided by the type of shock and haemodynamic parameters in individual cases. The outcome depends on the readiness of the clinician to proper resuscitation, identify the underlying cause and starting the cause specific management.

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Resuscitation of Pregnant Women

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Maternal collapse during pregnancy and puerperium is a life threatening event that can have varying aetiologies. It is defined as an acute event involving the cardiorespiratory system and/or brain, resulting in reduced/absent conscious levels and potentially death at any sage of pregnancy and upto 6 weeks postpartum. The exact incidence of maternal collapse is not known as morbidity data is not routinely collected in a standardized manner. As maternal collapse is a rare event which can have devastating consequences, all obstetricians should have skills for effective resuscitation.

Maternal collapse resuscitation should follow the standard approach with some modifications for maternal physiology specially relief of aortocaval compression due to gravid uterus, Fig 1. This can be achieved by manually displacing the uterus laterally rather than tilting the patient. Apply maximal leftward push to right upper border of uterus to achieve a displacement of 1.5 inches from midline.

In women over 20 weeks of gestation or fundal height above the umblicus, if there is no response to correctly performed CPR within 4 minutes of maternal collapse then a perimortem cesarean section should be undertaken to assist maternal resuscitation. Ideally, this should be achieved within 5 minutes of the collapse. This should be performed wherever woman has collapsed and resuscitation is taking place. It should be clear that the procedure is primarily performed to assist maternal resuscitation rather than to save the fetus.

The latest systematic review to study the efficacy of PMCS by Einav et al has reported the outcome of 94 women. PCMS was beneficial to fetal and maternal survival in 31.7% of cases and no harm was reported in any of these women. When analysing maternal outcome, 54.3% of women survived until hospital discharge and 78.4% of women survived with good to moderately impaired neurological outcome. It also showed that maternal outcomes were more favourable if PCMS was performed within 10 minutes of arrest (OR 7.42; $P < 0.05$). Neonatal survival was also associated with a shorter mean cardiac arrest to delivery time. The reality is that PMCS is not usually started, nor is the fetus delivered, within the ideal 4- and 5-minute timeframes. Even when these time limits are crossed, there is still possibility of maternal and fetal benefits and if resuscitation attempts continue, PMCS should still be performed even when the delay is 30 minutes or more

During CPR

Post Cardiac Arrest Treatment

- Recovery position (left lateral position)
- Check ABCD
- Maintain IV access, oxygen
- Secure airway if needed
- Check fetal well being
- Recognise & treat causes

Respiration Failure

If carotid pulse is palpable but no breathing is present- Immediately start Bag and mask ventilation with 100% oxygen at >15 l/min after checking for airway obstruction.

Unconsciousness with Palpable Carotid Pulse with Patient Breathing

Put patient in recovery position by following steps: With the woman lying on her back, extend her arm nearest to you at a right angle to their body with their palm facing up. Take the other arm and fold it so the back of her hand rests on the cheek closest to you, and hold it in place. Use the other hand to bend the woman's knee farthest from you to a right angle and carefully roll the woman onto their side by pulling on the bent knee. The bent arm supports the head and the extended arm prevents rolling away of woman, Fig 2. Care should be taken to keep the bent leg at a right angle. Open the airway by gently tilting woman's head back and lift the chin to make sure and check that the airway is not blocked. Don't leave the patient unattended till airway is secured by intubation.

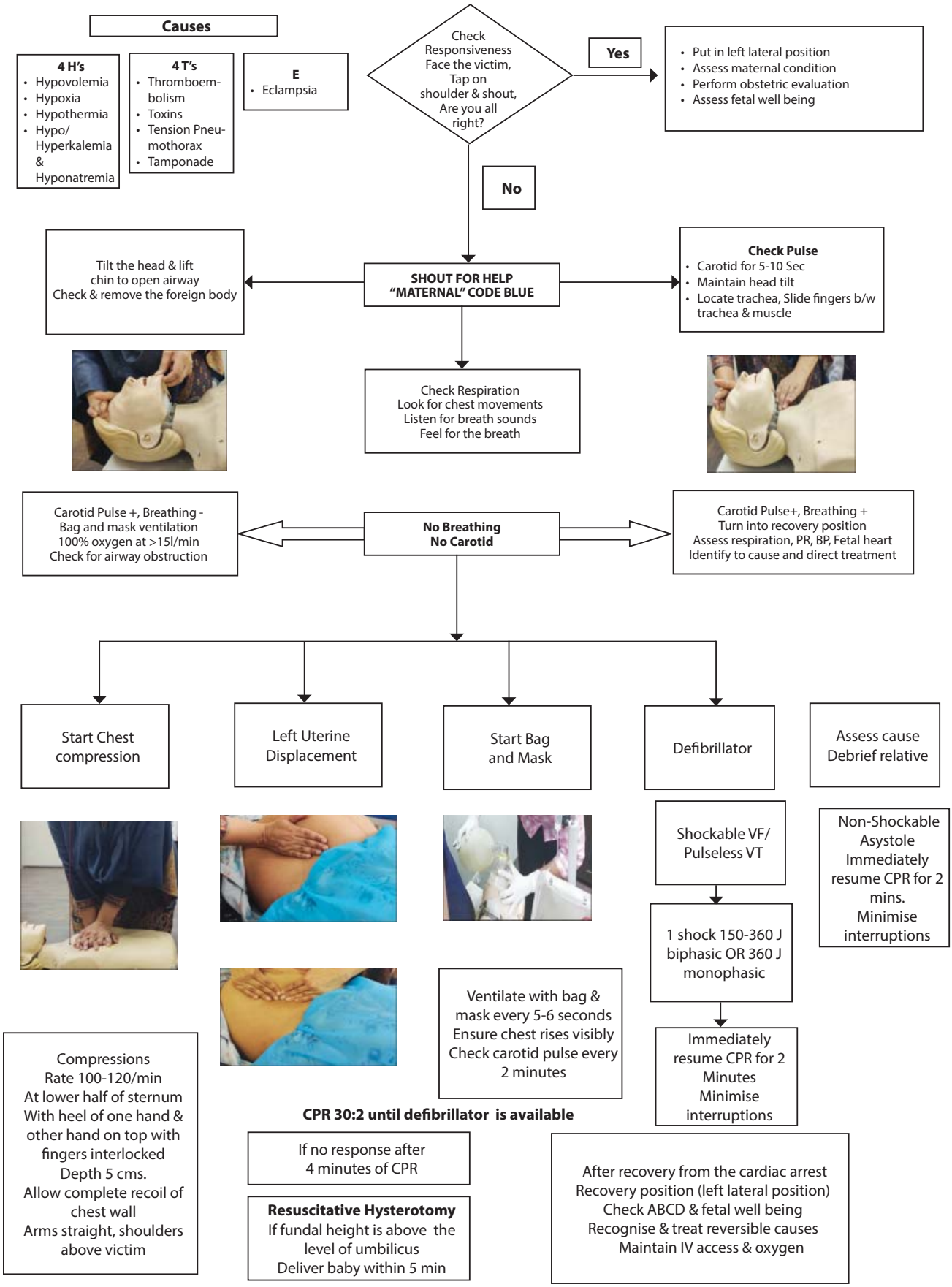

Fig 1: Steps in Resuscitation of Pregnant woman

Fig 2: Recovery Position

Suggested Reading

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Calendar of Virtual Monthly Clinical Meetings 2021-22

28th May, 2021	B L Kapoor Hospital
25th June, 2021	All India Institute of Medical Sciences
30th July, 2021	Sitaram Bhartia Hospital
3rd September, 2021	Army Hospital (Research & Referral)
24th September, 2021	Deen Dayal Upadhyay Hospital
29th October, 2021	PGIMSR & ESI Hospital
19th - 21st November, 2021	43rd Annual Conference
26th November, 2021	MAMC & Lok Nayak Jai Prakash Narayan Hospital
7th January 2022	Sir Ganga Ram Hospital
28th January, 2022	ABVIMS & Dr Ram Manohar Lohia Hospital
25th February, 2022	UCMS & Guru Tek Bahadur Hospital
25th March, 2022	VMMC & Safdarjung Hospital
29th April, 2022	LHMC & Smt. Sucheta Kriplani Hospital
27th May, 2022	Apollo Hospital

Carle's Obstetric Early Warning Score as a Screening Tool for Predicting Poor Perinatal Outcome: A Prospective Observational Study

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Abstract

Background: Early Warning Systems (EWS) involve serial measurements of physiological parameters with criteria (trigger) to timely identify patients at risk of complications. EWS in obstetrics have been used to predict poor maternal outcome. Carle designed statistically based clinically modified obstetric early warning score (Carle's OEWS). The present study evaluates utility of Carle's Obstetric Early Warning Score as a screening tool for predicting poor perinatal outcome.

Material & Methods: A prospective observational study was conducted among 1250 obstetric women with period of gestation ≥ 28 weeks admitted in the labor wards of a tertiary center over 18 months from 1 November, 2017 to 30 April, 2019. Physiological parameters of OEWS were recorded and aggregate score calculated at admission and at regular intervals thereafter, till discharge. Scores were analyzed using Statistical Package for Social Sciences (SPSS) version 21.0 (licensed).

Results: Area Under Receiver Operating Characteristics (AUROC) Curve of OEWS for predicting poor perinatal outcome is 0.896 with a significant p-value <0.001. It is seen that at an aggregate score of 3.5 MEOWS is 88.9% sensitive and 80.5% specific in predicting poor prognosis of the baby with a positive predictive value of 17.5% but a negative predictive value of 99.4%.

Conclusion: Carle's OEWS is a useful screening tool for predicting perinatal outcome and can be used in labor wards to ensure timely intervention. Poor fetal outcome at lower MEOWS score suggests that mother and fetus act as a single unit and before maternal deterioration becomes evident, baby is already compromised. Thus, one needs to be vigilant even at lower scores.

Keywords: Obstetric Early Warning Score; Carle's Obstetric Early Warning Score; Critical Care Unit Admission; Perinatal Death; Stillbirth; Neonatal Death.

Introduction

Maternal mortality during pregnancy or postpartum period is an unfortunate event. It has long term interlinked, intergenerational and extensive impact both for the immediate family and the wider community.[1,2] Despite advances in medical science and extensive efforts by governments across the world, maternal mortality continues to be high. Maternal deterioration proceeds sequentially through morbidity, severe morbidity, nearmiss event and mortality.[3] Early Warning Systems (EWS) record physiological parameters at regular intervals and involve timely intervention at predefined trigger points to disrupt the chain of adverse outcome. Physiological changes in pregnancy prevent extrapolation of EWS used for general population to obstetric population.[4]

Confidential Enquiry into Maternal and Child Health, CEMACH 2003-05 first designed Modified Early Obstetric Warning System (MEOWS) for obstetric patients based on expert opinions and continued to recommend its use in its subsequent reports.[5] Thereafter, the system was validated by several authors for different maternal outcomes.[6-10] In 2013, Carle et al statistically designed and clinically modified an aggregate score based obstetric early warning system (Carle's OEWS) for use in labor wards.[11] They retrospectively validated the score in obstetric patients using parameters of first 24 hours of Intensive Care Unit (ICU) admission and subsequently the score was validated externally by Paternina et al.[12]

Different adaptations of the original CEMACH MEOWS are in use in different regions of the world that vary in parameters and cut-offs.[13-17] The use of OEWS appears promising for early identification of a deteriorating obstetric patient but more evidence and standardization is required.[18] However, there is scant literature studying the role of obstetric warning scores with perinatal outcomes. The aim of the present observational study was to prospectively

evaluate Carle's OEWS as a bedside screening tool among 1250 pregnant and postpartum women for prediction of perinatal outcomes.

Material & Methods

A prospective observational study was conducted in the Department of Obstetrics and Gynaecology, a tertiary care referral center of Delhi, over 18 months period from 1 November, 2017 to 30 April, 2019 after institutional ethical clearance. The study included 1250 obstetric women with period of gestation ≥ 28 weeks admitted in labor wards. Informed consent was taken. Pregnant patients requiring operative interventions or critical care at admission were excluded.

Carle's OEW score (Table 1) was calculated by the treating physician for all subjects at admission, then 4 hourly in the first stage of labor, half hourly in the second stage of labor, half hourly for first 2 hours after delivery and then 12 hourly till discharge. All seven physiological parameters of Carle's OEWS were documented: Systolic Blood Pressure (SBP), Diastolic Blood Pressure, Respiratory Rate (RR), Heart Rate (HR), FiO_2 required to maintain $SpO_2 \geq 96\%$, Temperature (TEMP), and Conscious Level. There were no missing entries. .

An aggregate score was calculated for each set of parameters at discharge by the primary investigator to ensure there was no bias. The highest score of all scores was taken for analysis. The patients were followed for perinatal outcomes. The study was purely observational and the management of the patients was according to the hospital protocols already in place.

All statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) version 21.0 (licensed). A p-value of <0.05 was considered statistically significant. Diagnostic test was used to calculate sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Area Under Receiver Operating Characteristic Curve was used to find out area under curve of Carle's OEWS (AUROC) for predicting perinatal outcome.

Results

The mean age of women participating in the study was 25 years ± 4.11.

Majority of women in the study were primiparous (43%) and about half of the patients were booked (49.6%). Being a tertiary care centre, there were 22.7% referrals.

Of 1250 births, 924 (73.9%) babies were term, 309 (24.7%) were preterm, while only 17 (1.36%) were postterm (Figure 1). In 70 births, liquor was meconium stained. 131 babies were growth restricted. 57 mothers had presented with decreased fetal movements.

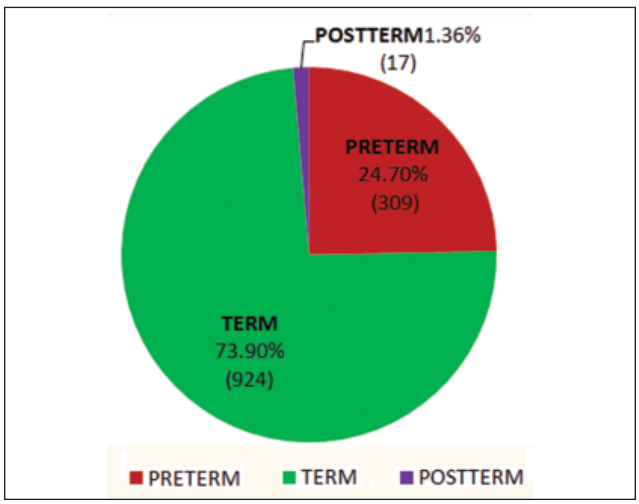

Fig 1: Distribution of Neonatal Births according to Maturity

Nursery admission was required in 228 babies (18.24%) of 1250. Of these, 57% mothers had MEOW score >3. Where babies did not require nursery admission, only 18% mothers had a MEOW score higher than 3 (Figure 2)

It was observed that 1162 (92.96%) pregnant women

Table 1: Carle's Statistically Designed, Clinically Modified and Internally Validated, Aggregate Weighted Obstetric Early Warning Score (Carle's OEWS)

Parameter	3	2	1	Normal	1	2	3
Systolic Blood Pressure, mm Hg (SBP)	<80	80-89		90-139	140-149	150-159	≥160
Diastolic Blood Pressure, mm Hg (DBP)				<90	90-99	100-109	≥110
Respiratory Rate/ min (RR)	<10			10-17	18-24	25-29	≥30
Heart Rate/ min (HR)	<60			60-110		111-140	≥150
$\%O_2$ required to maintain $SpO_2 \geq 96\%$				Room air	24-39%		≥40%
Temperature, ºC (TEMP)	<34.0		34.0-35.0	35.1-37.9	38.0-38.9		≥39
Conscious level				Alert			Non alert

had live newborns, while adverse perinatal outcome were seen in the rest. Of these, 34 (2.72%) mothers had stillbirths and 54 (4.32%) had neonatal deaths (Figure 3).

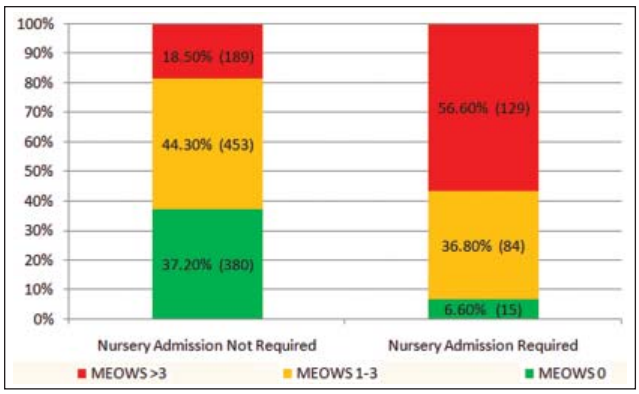

Fig 2: MEOW score of mothers with babies not requiring nursery admission and those requiring nursery admission.

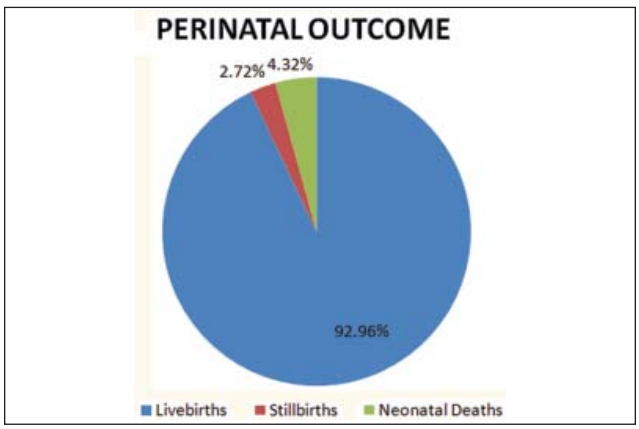

Fig 3: Distribution of Neonatal Births according to Perinatal Outome.

It was seen that as the MEOW score increased, perinatal outcome worsened. At MEOW score of 0, there were all livebirths. At score of 1 to 3, there was only 1 (0.18%) stillbirth and 6 (1.11%) neonatal deaths. At score of 4-6, stillbirths were 9.70% (24) and neonatal deaths were 15.30% (38). While at a score >6, there were 12.6% (9) stillbirths and 14% (10) neonatal deaths (Figure 4).

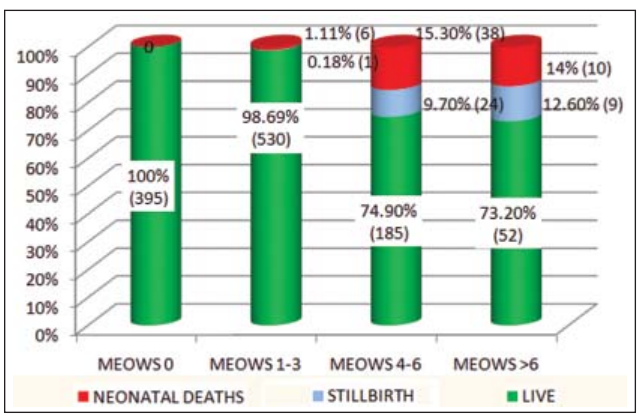

Fig 4: Perinatal Outcome at Different MEOW Scores.

Admission in critical care unit (CCU) was required by 76 women. While only 4.9% mothers with livebirths required critical care unit (CCU) stay, 29.4% mothers with stillbirths and 16.7% mothers with neonatal deaths required CCU admission (Figure 5). CCU admission is taken as a surrogate marker for poor maternal outcome.

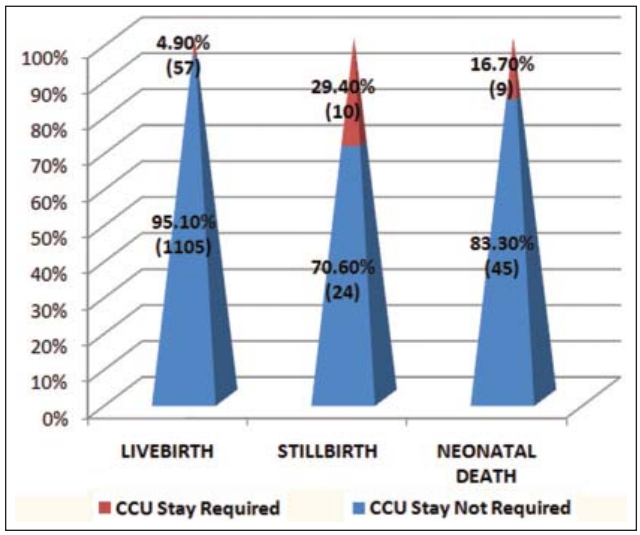

Fig 5: Need of CCU in Mothers with different Perinatal Outcome

The Receiver Operator Characteristic Curve (Figure 6) for prediction of fetal/ neonatal death by MEOWS score shows AUROC of 0.896, which was found to be significant with a p-value of 0.001 (CI-0.865-0.926). At an aggregate score of 3.5, MEOWS is 88.9% sensitive and 80.5% specific in predicting poor prognosis of the baby with a positive predictive value of 17.5% and a negative predictive value of 99.4% (Table 2).

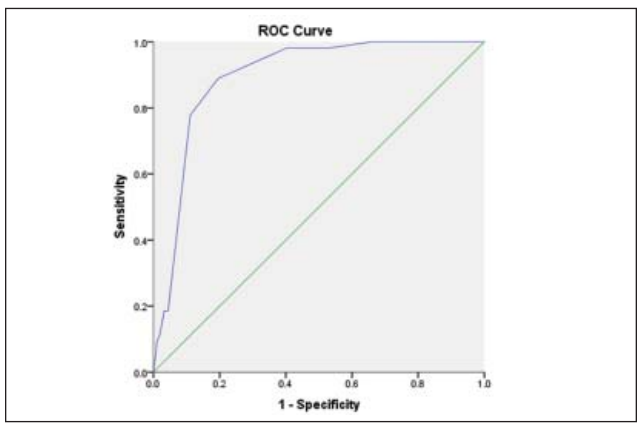

Fig 6: ROC Curve Showing Sensitivity and Specificity of MEOWS in Predicting Perinatal Mortality

Area Under the Curve (AUROC)	Std Error	p value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.896	0.016	<0.001	0.865	0.926

Table 2: Table Showing Sensitivity and Specificity of Carle's MEOWS in Predicting Perinatal Mortality

Positive if Greater Than or Equal To	Sensitivity	Specificity
-1.00	100.00%	0.00%
0.50	100.00%	33.99%
1.50	98.15%	46.90%
2.50	98.15%	59.72%
3.50	88.89%	80.46%
4.50	77.78%	88.90%
5.50	37.04%	93.46%
6.50	18.52%	95.61%
7.50	18.52%	96.73%
8.50	11.11%	98.11%
9.50	9.26%	98.97%
10.50	3.70%	99.48%
11.50	3.70%	99.57%
12.50	1.85%	99.83%
14.00	0.00%	100.00%

Cut-off = 3.5				
Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnostic Accuracy
88.9%	80.5%	17.5%	99.4%	80.8%

Discussion

In the present study, it was seen that there were no perinatal deaths in the nontriggered group, while as the trigger score of MEOW system increased perinatal mortality increased. Stillbirth was seen in only 0.18% (1) of MEOW score 1-3, 9.70% (24) in group with MEOW score 4-6, and highest 12.60% (9) in group with MEOW score >6. Similar trend was seen for neonatal mortality. There were only 1.11%(6) neonatal deaths in group with MEOW score 1-3, 15.30% (38) in group with MEOW score 4-6, and 14% in group with MEOW score>6. At p-value of <0.001, this difference is significant.

Similar, observations were seen in Singh A. et al's study. Neonatal death was seen in 2.8% of triggered and 2.6% of non-triggered group. IUD was seen in 3.9% of triggered and only among 1.3% of non-triggered group. At a p- value of 0.053, this difference is significant.[7]

The AUROC for prediction of poor fetal/neonatal outcome by MEOWS score is 0.896, which was found to be significant with a p-value of 0.001 (CI-0.865-0.926).

In a study by Paternina et al, AUROC for prediction of maternal mortality by using Carle's MEOWS system is 0.84.[18] It can be said that Carle's MEOWS score can be used not only for prediction of poor maternal outcome, but also poor perinatal outcome.

It was seen that at an aggregate score of 3.5 MEOWS is 88.9% sensitive and 80.5% specific in predicting poor prognosis of the baby with a positive predictive value of 17.5% and a negative predictive value of 99.4%. Poor fetal outcome at lower MEOWS score suggests that mother and fetus act as a single unit and before the maternal deterioration becomes evident, baby is already compromised. Thus, one needs to be vigilant even at lower scores. It can be concluded that fetal deterioration not only indicates poor perinatal outcome, but forewarns about impending maternal deterioration and the aggregate score of Carle's MEOW system can act as a useful tool to quantify these changes.

A robust sample size, a prospective study design and the use of a scientific obstetric warning score add to the strengths of the present study.

Further interventional studies are recommended in different population settings to determine the utility of Carle's OEWS as a screening tool for predicting poor fetal-maternal outcome using the escalation protocol suggested by Carle and the utility of different aggregate scores.

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Can Placenta Accreta Index Predict Maternal Outcomes?

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Abstract

Introduction: Placenta accreta spectrum (PAS) incorporating adherent and invasive placenta, is a clinical entity with grave complications. Predicting the severity of maternal outcomes can be instrumental in apposite operative planning, including adequate allocation of resources like the number of blood products needed and ICU beds, especially in LMIC like India. Placenta accreta index Score is one such tool to predict PAS, and can be utilized for decreasing the health care burden.

Material & Methods: This prospective study was conducted on 71 women with history of previous cesarean and placenta Previa, amongst whom 30 were found to have PAS. The subjects were then evaluated by PAIS and number of blood products transfused and days of ICU care required was recorded. Association of maternal outcomes with PAIS was also evaluated.

Results: Spearman rank coefficient for correlation of PAIS was found to be 0.745, 0.708, 0.697 for blood loss, blood products transfused and days of ICU care respectively, indicating a positive correlation of these with PAIS.

Conclusion: PAIS has a strong predictive value for severity of maternal outcomes in patients with PAS.

Keywords: Placenta accreta spectrum, PAS, Placenta accreta index score, PAIS, maternal outcome

Introduction

Placenta accreta spectrum (PAS) includes placenta accreta, increta and percreta, according to depth of placental villi invasion. Any women with PAS can have torrential bleeding, especially on the operating table if manual removal/separation of placenta is attempted. This can lead to unacceptably high mortality, besides complications like hemorrhagic shock, Multi-organ dysfunction, need for multiple transfusions/ICU care, etc.[1] It thus becomes imperative to ensure availability of multiple blood products at time of surgery in PAS. Apart from this, higher probability of surgical complications necessitates presence of a urogynaecologist and pelvic surgeon besides experienced obstetrician.[2,3] Thus, an accurate antenatal diagnosis and estimation of severity of anticipated complications is essential for ensuring multi-disciplinary care to these patients and reducing their morbidity.

Placenta accreta index score (PAIS) is one such tool utilizing clinical and ultrasound findings to predict PAS in women with previous cesarean and placenta previa.[4] Though the diagnostic accuracy of PAIS is well established by various researchers in past[5-7], but its association with maternal outcomes has not been evaluated much. Hence this study was conducted to gauge the correlation of PAIS with severe maternal outcomes, that can lead to adept operative planning, including adequate allocation of resources like the number of blood products needed and ICU beds, especially in LMIC like India.

Material & Methods

This prospective study was conducted in the Department of Obstetrics and Gynaecology, Safdarjung hospital from 1st June 2020 to 31st May 2021 in which 71 women with history of previous cesarean and placenta previa were recruited, and subjected to antenatal evaluation by the PAIS after 28weeks of gestation. Per-operatively, the blood loss was estimated by counting the number of soaked mops, spillage of blood on floor and amount of blood in the suction machine. The total number of blood products transfused in each case was also recorded. All women were followed up post-operatively till discharge. Number of days of ICU stay was logged. The data was entered in MS EXCEL spreadsheet and analyzed using SPSS 27.0 (Statistical Package for Social Sciences).

Results

Amongst the 71 women enrolled in the study, 30 were found to have PAS disorders. These women (mean of 2803.33 ± 900.38 ml) had higher blood loss than those without PAS (940.24 ± 488.26 ml). The range of total blood loss varied from 1000-4500ml

in the study populace. The Correlation coefficient of PAIS and total blood loss was found to be 0.745 by Spearman rank correlation (Figure 1, Table 1). This was a statistically significant correlation.

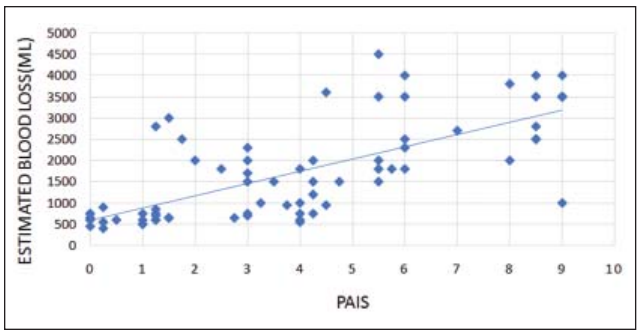

Fig 1: Correlation of estimated blood loss with PAIS

Table 1: Correlation between PAIS and maternal outcomes

PAIS	Estimated blood loss(ml)	Total blood/ blood products transfused	Post op ICU stay (in days)
Spearman Rank Correlation coefficient	0.745	0.708	0.697

Mean of 12 ± 4.29 units of blood products was transfused in patients with PAS with a variation of 6-19 units. The Spearman rank Correlation coefficient was found to be 0.708 between PAIS and number of blood products transfused (Figure 2, Table 1). This shows a statistically significant correlation between PAIS and units of blood products transfused and increase in score is positively correlated with it.

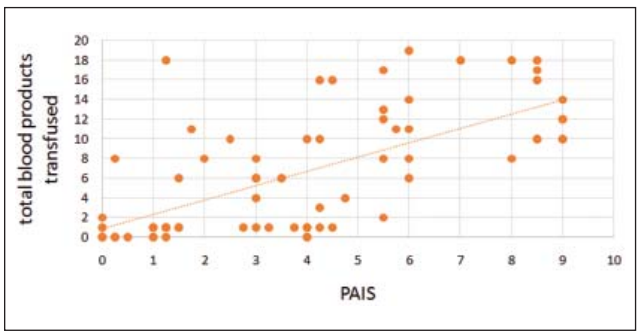

Fig 2: Correlation of total blood/blood products transfused with PAIS

On an average women with PAS stayed in ICU for 3.7 ± 1.8 days while those without PAS 0.51 ± 1.25 days. Range of ICU stay of study population varied from 1 to 7 days. The Spearman rank Correlation coefficient of 0.697 suggests that more the PAIS, more is the probability of patient to have a longer postoperative ICU stay (Figure 3,Table 1).

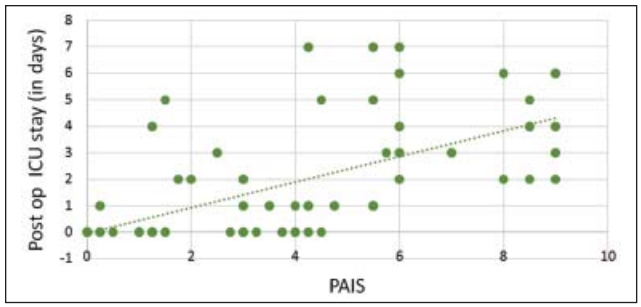

Fig 3: Correlation of post op ICU stay (in days) with PAIS

Discussion

The study postulated that women with PAS had greater blood loss, requiring more number of blood product transfusion, when contrasted with those without PAS. However, there was a huge variation of 1000-4500ml of total blood loss and 6-19 units of blood and blood products transfused between the two groups. Also, women with higher score of PAIS had greater blood loss, and hence more transfusion. These findings were similar to the observations of Samosir et al (mean blood loss in PAS=2622ml, mean PRBC transfused =387.78 ml, mean FFP transfused= 68.89 ml). However, study by Hamed et al, 84.21% of patients with PAS disorder required massive blood transfusion and 52.63% patients with PAS. These women thus need to be forewarned about extensive blood loss, and counselled regarding massive blood transfusion, besides adequate preparedness is warranted when dealing with such women, especially for arranging adequate blood products

The same results were reverberated for the number of days of ICU stay of women with higher PAIS. These were in consonance with the work of Samosir et al (10 %) and Hamed et al Hence women with very high PAIS require tertiary care with arrangement of ICU care beds in advance, and relatives are required to be briefed accordingly. In the study by Happe et al, they found that patients who underwent cesarean hysterectomy had a higher PAIS than those not requiring hysterectomy (9 versus 1.75; $P < .001$).[8]

Since none of the past investigators had correlated the PAIS to the maternal outcomes, this made our study unique and essential. Nonetheless, the limitation of our study is limited sample size and hence more studies and bigger sample size is needed to support the hypothesis.

Conclusion

The placenta accreta index score may be useful for predicting severity of maternal outcomes in women

with previous cesarean and placenta previa. The information drawn from this can be used for timely referral of a patient with PAS disorder to a tertiary level, multidisciplinary facility and also for optimum allocation of resources within the health facility.

Recommendations

All women with placenta previa with history of previous CS should undergo screening for PAS disorders and all such cases should be managed at a tertiary care center by a multidisciplinary team.

Since higher score represents a greater chance of maternal morbidity. Hence, a greater number of blood products should be kept ready in these cases and ensure availability of ICU beds.

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Journal Scan

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Intravenous Infusion Route in Maternal Resuscitation: A scoping review

Nakamura E, Takahashi S, Matsunaga S, Tanaka H, Furuta M, Sakurai A

Japan Resuscitation Council (JRC), Guideline Editorial Committee. BMC Emerg Med. 2021 Dec 3;21(1):151.

Background: The concept that upper extremities can be used as an infusion route during cardiopulmonary resuscitation in pregnant women is a reasonable recommendation considering the characteristic circulation of pregnant women; however, this method is not based on scientific evidence.

Objective of the review: We conducted a scoping review to determine whether the infusion route should be established above the diaphragm during cardiopulmonary resuscitation in a pregnant woman.

Discussion: We included randomized controlled trials (RCTs) and non-RCTs on the infusion of fluids in pregnant women after 20 weeks of gestation requiring establishment of an infusion route due to cardiac arrest, massive bleeding, intra-abdominal bleeding, cesarean section, severe infection, or thrombosis. In total, 3150 articles from electronic database were extracted, respectively. After title and abstract review, 265 articles were extracted, and 116 articles were extracted by full-text screening, which were included in the final analysis. The 116 articles included 78 studies on infusion for pregnant women. The location of the intravenous infusion route could be confirmed in only 17 studies, all of which used the upper extremity to secure the venous route.

Conclusion: Pregnant women undergo significant physiological changes that differ from those of normal adults, because of pressure and drainage of the inferior vena cava and pelvic veins by the enlarged uterus. Therefore, despite a lack of evidence, it seems logical to secure the infusion route above the diaphragm when resuscitating a pregnant woman.

Effect of Antithrombin III Among Patients with Disseminated Intravascular Coagulation in Obstetrics: A Nationwide Observational Study in Japan

Iwasaki Y, Ohbe H, Shigemi D, Fushimi K, Yasunaga H

BJOG. 2021 Sep 21.

Objective: Pregnant women may develop disseminated intravascular coagulation (DIC), possibly resulting in massive maternal haemorrhage and perinatal death. The Japan guideline recommends use of antithrombin III (ATIII) for DIC in obstetrics; however, its effect remains uncertain. The present study aimed to investigate the effect of ATIII for DIC in obstetrics, using a national inpatient database in Japan.

Design: Nationwide observational study.

Setting: Japan.

Population: We used the Diagnosis Procedure Combination inpatient database to identify patients who delivered at hospital and were diagnosed with DIC from July 2010 to March 2018.

Methods: Propensity score matching analyses were performed to compare in-hospital maternal mortality and hysterectomy during hospitalisation between users and non-users of ATIII on the day of delivery.

Main Outcome Measures: In-hospital mortality, hysterectomy.

Results: A total of 9920 patients were enrolled, including 4329 patients (44%) who used ATIII and 5511 patients (56%) who did not use ATIII. One-to-one propensity score matching created 3290 pairs. In-hospital maternal mortality did not differ significantly between the propensity-matched groups (0.3% in the ATIII group versus 0.5% in the control group; odds ratio 0.73; 95% CI 0.35-1.54). A significantly lower proportion of patients in the ATIII group, compared with those in the control group, underwent hysterectomy during hospitalisation (5.3% versus 8.7%; absolute risk difference -2.9%; 95% CI -4.2 to -1.6%).

Conclusions: Although the present study did not show a mortality-reducing effect of ATIII for patients with DIC in obstetrics, it may have clinical benefit in terms of reducing the number of patients undergoing hysterectomy.

Determinants of Maternal Mortality in a Critical Care Unit: A Prospective Analysis

Kumar R, Gupta A, Suri T, Suri J, Mittal P, Suri JC
Lung India. 2022 Jan-Feb;39(1):44-50.

Introduction: An admission of a pregnant woman to an intensive care unit (ICU) is considered as an objective marker of maternal near miss. Only a few studies from the Indian subcontinent have reported on the ability of ICU scoring systems in predicting the mortality in obstetric patients.

Methods: A prospective analysis of all critically ill obstetric patients admitted to the critical care department was done.

Results: In the period between April 2013 and September 2017, there were 101 obstetric admissions to the critical care ICU. Of these, 82 patients (81.2%) were discharged from the hospital, 18 patients (17.8%) died, and one left against medical advice. The common diagnoses seen in these patients were cardiac failure (n = 39; 38.6%); pregnancy-induced hypertension (n = 26; 25.7%); acute respiratory distress syndrome (n = 20; 19.8%); intra-abdominal sepsis (n = 19; 18.8%); tropical diseases (n = 19; 18.8%); and tuberculosis (n = 13; 12.9%).When we compared the survivors with the nonsurvivors, a higher severity of illness score and a low PaO_2/FiO_2 were found to increase the odds of death. The area of distribution under the receiver operator characteristic curve was 0.726 (95% confidence interval [CI] = 0.575-0.877) 0.890 (95% CI = 0.773-1.006) 0.867 (95% CI = 0.755-0.979), and 0.850 (95% CI = 0.720-0.980) for the $PaO2/FiO_2$. Simplified Acute Physiology Score (SAPS) II, Sequential Organ Failure Assessment and Acute Physiology and Chronic Health Evaluation (APACHE) II score, respectively, for predicting mortality. The standardized mortality ratio was better with SAPSII than with APACHE II.

Conclusions: Cardiac dysfunction is a leading cause of ICU admission. Obstetric patients frequently require ventilatory support, intensive hemodynamic monitoring, and blood transfusion. The APACHE II score is a good index for assessing ICU outcomes.

Proceedings of AOGD Monthly Clinical Meeting held at Sir Ganga Ram Hospital, New Delhi on 7th January, 2022

Nonpuerperal Uterine Inversion: Laparascopic Management

Mamta Dagar, Punita Bhardwaj

Uterine Inversion is a rare entity. Non puerperal Uterine Inversions (NPUI) are even rarer accounting for only 16% of all inversion cases and are mostly associated with submucous myoma. We report here a case of 41 year old lady presented with some mass coming per vaginum since last 3 months, noticed suddenly while doing yoga and was painless. It was associated with irregular & heavy bleeding per vaginum and discharge. There was history of 8 units blood transfusion in last 3 months in view of severe anaemia. She was diagnosed to have fibroid polyp on ultrasound 14 months back during routine medical checkup. There was history of heavy menstrual bleeding since last 2 years. She had 2 normal vaginal deliveries with no significant personal, past and family history. She had normal BMI (26.7). Her systemic examination was unremarkable. Local examination showed a smooth, dark red mass protruding out of introitus with a pale firm mass (fibroid polyp) of 5*3 cm attached to base, bleeding on touch and non reducible.

On imaging, MRI findings revealed a heterogeneous mass in the vagina with uterine body in a U shape and target sign was observed where uterine corpus was surrounded by cervix and vaginal fornix.

Based on history, clinical examination and imaging, diagnosis of Uterine inversion due to submucous myoma was made and she was counselled for surgical management. As she was not willing for any conservative uterine surgery, decision for laparoscopic hysterectomy was taken after informed consent.

During surgery, first the correction of inversion by Haultain's method (cutting the constriction ring posteriorly) after injecting dilute vasopressin followed by pulling of the tissue to correct the uterine inversion and then laparoscopic hysterectomy with bilateral salpingectomy and right ovarian cystectomy was performed under GA. Her post op period was uneventful and she was discharged after 48 hours.

Histopathology examination of tissue suggested extensive ulceration with features of squamous metaplasia, chronic cervicitis, leiomyoma, unremarkable tubes and corpus luteum cyst.

Management of acute or chronic non puerperal inversion uterus is surgical, which can be done via abdominal, vaginal or laparoscopic routes. There are several different methods described in literature- Huntington's method, Haultain's operation, Spinenell's operation and Kustner's operation. The clinician depending on the causative pathology, clinical presentation, desire for future fertility and surgical expertise should select the best surgical approach. In the era of minimal invasive surgery, laparoscopic route is preferred due to minimal incision, less blood loss and pain and faster recovery but it should be done by experienced surgeon as altered anatomy poses many challenges.

Hypereactio Leutanalis in Pregnancy

Sharmistha Garg

34 years old G2A1 with 35+5 weeks POG with DCDA twin pregnancy came to labour room with labour pains. She was a known case of PCOD and also gave history of 5-6 cycles of IUI and last IUI was done a year back. This was a spontaneous conception and her ANC work up revealed IHCP (serum bile acid 21.69). She gave history of hoarseness of voice, acne and hirsutism which started at around 26 weeks POG. Her ANC ultrasound at 32 weeks revealed B/L large cystic ovaries with multiple enlarged thin wall cysts with thick septae and anechoic cystic fluid with raised vascularity on Doppler suggestive of ovarian hyperstimulation syndrome. She underwent LSCS in view of first non vertex presentation and delivered a female baby of 2.1 kg and a male baby of 2.1 kg. Intraoperatively ovaries were found enlarged with multiple loculated cysts with smooth capsule suggestive of hyper reaction leutinalis. Post operatively patient was followed up with serial ultrasound and B/L ovaries showed gradual decrease in size of both the ovaries and complete regression occurred after 4 months of delivery.

Misplaced CuT in Urinary Bladder

Renuka Brijwal

34 years old women, P2L2 presented with complaint of burning micturition with occasional blood in urine since 1.5 months. History of post partum IUCD insertion 5 years back and she never felt CuT thread vaginally post insertion. USG was done which showed displaced IUCD and vertical limb piercing anterior myometrium with its lower end piercing the bladder wall and reaching the bladder lumen. She was planned for hysteroscopic / cystoscopic removal of IUCD in OT.

On hysteroscopy Horizontal limb of IUCD was visible in uterine cavity with vertical limb penetrating the myometrium removed tried but failed. Cystoscopy done next, vertical limb was penetrating bladder mucosa and entering the bladder lumen, limb removed cystoscopically and foley's catheter inserted. Post operative period was uneventful. After 3 week MCU was done and it was normal, so catheter was removed and patient sent back home.

Torted Endometrioma with Large Uterine Fibroid at 54 years

Kanika Jain

Mrs. X, 54 years old perimenopausal lady came to SGRH OPD with complaints of acute pain lower abdomen since 15 days with difficulty in micturition. She also complained of irregular and heavy menstrual cycles since 2 years associated with severe congestive dysmenorrhea. She attained menarche at age of 13 years and her last menstrual period was on 1/10/21. She had two FTNVD with last child birth 24 years back.She was diagnosed with anemia recently. Her mother was both diabetic and hypertensive.

On examination she had moderate pallor. Per abdomen examination revealed a large firm mass felt up to 28-30 week size with another firm to cystic mass felt on right side up to 16-18 weeks separated from the above mass. On per vaginum examination uterus was retroverted, deflexed to right, bulky with restricted mobility lying between the above mentioned masses. On blood investigation, her Hb was 8 gm% and increase Ca125- 53.8 was raised. Rest WNL. MRI reported bulky uterus with multiple small intramural fibroid. A large subserosal fibroid 12x9 cm with hyaline degeneration. A well defined hyperintense oblong lesion of size 13x7 cm in pelvis ?TO mass with torsion, ?Hematosalpinx with benign mucinous cystadenoma.

Patient was prepared for laparoscopy and proceed after adequate counseling and explained them various possible differential diagnosis. Patient was insistent on surgery being performed by laparoscopic route only even in case of suspected malignancy. Hence patient was taken up for laparoscopy after PAC clearance and written informed consent. On laparoscopy per op findings were, omentum was covering the large left anterofundal fibroid 20x15 cm. After separating the omentum another oblong mass was seen in the pelvis 20x10 cm extending from left IP ligament to right IP ligament. This left TO mass obscured the pelvic viscera and was twisted twice over the IP ligament, bluish black in colour and had adhesion with anterior abdominal wall, bladder, bowel and uterus. Pedicle of the fibroid ligated with transfixing suture and fibroid excised. Uterus was 12-14 weeks size with right antero- lateral fibroid 4x 4 cm, posterior wall fibroid 3x3 cm and multiple small intramural fibroids apart from the large 20x15 cm subserosal fibroid. Right tube and ovary was normal. Left ovary was not visualized separately from TO mass. After Adhesiolysis and separating the masses total laparoscopy hysterectomy with bilateral salpingo-oophrectomy was done ligating the vascular pedicles. Large subserosal fibroid was morcellated with power morcellation and fibroid pieces were taken out and sent for HPE. Left TO mass with uterus with cervix with right tube and ovary were retrieved vaginally in an endobag and sent for HPE.

Postoperative period was uneventful and no blood was transfused, patient was discharged on 3 rd postoperative day in stable condition. Her HPE report revealed atrophic endometrium with benign endometrial polyp. Myometrium was adenomyotic with leiomyomata with chronic cervicitis, right ovary was unremarkable, right fallopian tube and mild chronic salpingitis, left TO mass showed chronic inflammation with extensive haemorrhage and haemorrhagic infarctive necrosis secondary to torsion. Haemosedrin laden macrophages noted with some endometrial glands. No granulomatous or neoplastic pathology were seen.

Cross Word Puzzle

Niharika Guleria[1], Rekha Bharti[2]
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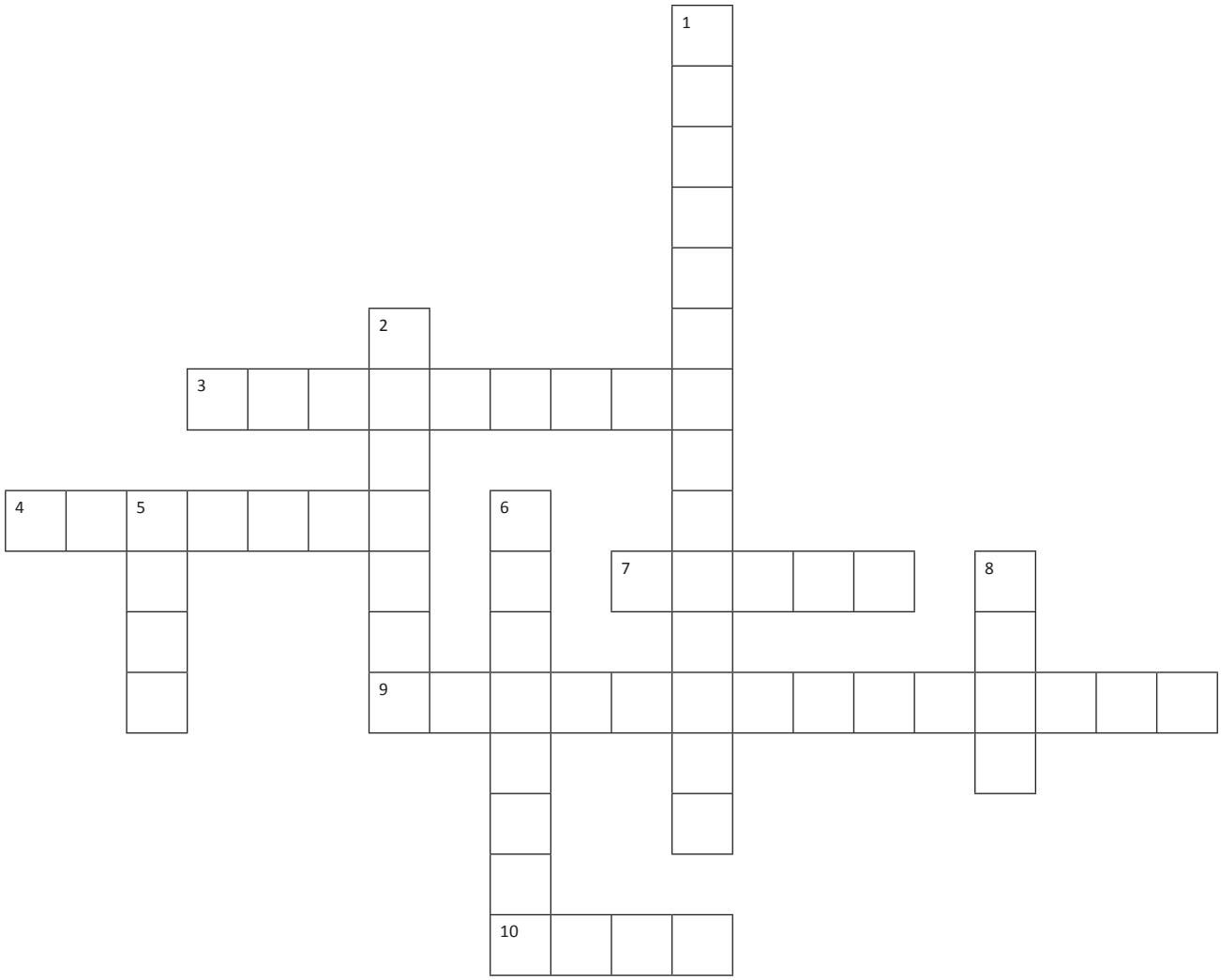


Across

3. First-line drug used in hypertensive crisis
4. Criteria used for diagnosis AFLP
7. Tennessee classification system used for diagnosis of which syndrome
9. Vasopressor of choice for septic shock
10. Score used for diagnosis of sepsis

Down

1. Drug of choice for pre-eclampsia associated with pulmonary edema.
2. Anticoagulant used in thrombotic DIC
5. Test used for evaluation of intrinsic pathway
6. First and a cardinal sign of IHCP
8. Other name for modified medical research council dyspnea scale

Mail the answers to editorsaogd2021@gmail.com. The correct answers and names of the three winners will be announced in the next issue.

Events Held in December 2021

S. No.	Date	Event	Time
1	02.12.2021	**"Tubal Corrective Surgeries; The Use of Endoscopy"** by Endoscopy Committee	6:00 - 8:00pm
2	03.12.2021	**AOGD Monthly Clinical Meeting** (November) at MAMC & LNJP Hospital	4:00 - 5:00 pm
3	04.12.2021	**AOGD Valedictory Ceremony**	6:00 - 8:00 pm
4	05.12.2021	**Camp** in Collaboration with Rotary Club Vasant Kunj and Rajeev Gandhi Cancer Hospital	9:00 am onwards
5	09.12.2021 10.12.2021	**"PPUICD Training in Private Sector"** in Association with FOGSI Family Welfare	2:30 - 3:00 pm
6	20.12.2021	PG Forum **"Diabetes in Pregnancy"** by LHMC and VMMC & Safdarjung Hospital	7:00 - 8:30 pm
7	23.12.2021	"Recent Advances in Gynecology & Book Launch", Webinar Medical Edge Series	7:00 - 8:00 pm
8	30.12.2021	**"Multidisciplinary Approach for Pelvic Pain"** in Association with Female Pelvic Pain Association, Delhi Chapter	5:00 - 7:00 pm
9	07.01.2022	**AOGD Monthly Clinical meeting (December)** at Sir Ganga Ram Hospital	4:00 - 5:00 pm

Events to be Held in January 2022

S. No.	Date	Event	Time
1	06.01.2022	"Current Updates in Screening for Down Syndrome- Obstetrician's Perspective" by Fetal Medicine Subcommittee	3:00 - 5:00pm
2	07.01.2022	AOGD Monthly Clinical Meeting at Sir Ganga Ram Hospital	4:00 - 5:00 pm
3	21.01.2022	CME "Adenomyosis" by Endometriosis Subcommittee	3:00 - 5:30 pm
4	22.01.2022	Translating Contraceptive Evidence into Clinical Practice in Association with FOGSI Family Welfare Committee	4:00 - 6:00 pm
5	25.01.2022	Evolve Programe a Joint Initiative of Delhi and Haryana Newer Concepts in Obstetrics and Gyneacology	3:00 - 5:00 pm
6	27.01.2022	Public Health Forum "Screening and Prevention of Cervical Cancer"	12:00 - 2:00 pm
7	27.01.2022	"Energy Sources in Endoscopy: An Imperative Art" by Endoscopy Subcommittee	6:00 - 8:00pm
8	28.01.2022	AOGD Monthly Clinical Meeting at ABVIMS & RML Hospital	4:00 - 5:00 pm
9	31.01.2022	Webinar on Research Methodology by AOGD	5:30 - 7:30pm

Events Held under the Aegis of AOGD in December 2021

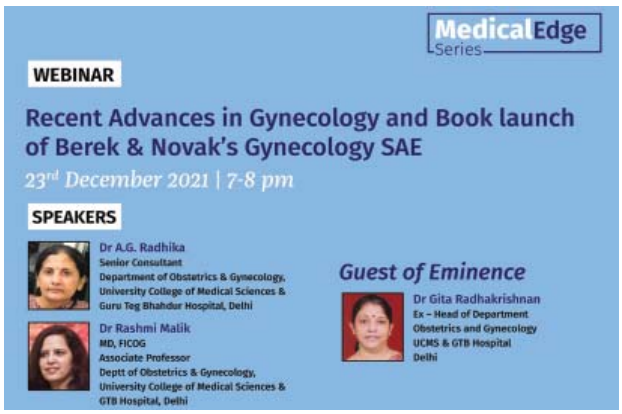
"Tubal Corrective Surgeries: The Use of Endoscopy"

AOGD Monthly Clinical Meeting, November

"AOGD Valedictory Ceremony"

Camp with Rotary Club Vasant Kunj and Rajeev Gandhi Cancer Hospital

"PPUICD Training in Private Sector"



PG Forum "Diabetes in Pregnancy by LHMC and VMMC & Safdarjung Hospital

"Multidisciplinary Approach for Chronic Pelvic Pain"

AOGD Monthly Clinical Meeting December

Association of Obstetricians & Gynaecologists of Delhi

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+ - In case of renewal, mention old membership number.
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AOGD SECRETARIAT

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43rd Annual Conference
Association of Obstetricians and Gynaecologists of Delhi
Conference Highlights

AOGD SECRETARIAT

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