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Content

Message from National President NARCHI

Dear NARCHI Members

Greetings!

It gives me immense pleasure to present the third issue of 'National NARCHI Periodical' to you. National Association of Reproductive and Child Health has been working with the Mission of safeguarding maternal health with a commitment to prevent maternal mortality. NARCHI envisions a future where all healthcare providers (HCPs) are equipped to save lives through comprehensive education and training. These periodicals are a step towards this.

This NARCHI periodical is dedicated to "Obstetric Critical Care". The need of an efficient obstetric critical care ecosystem in India is being felt as never before. The profile of our mothers is changing and the incidence of high-risk pregnancies is on the rise. There is a huge gap in the knowledge and preparedness of HCPs for the same. The theme for the periodical was conceived by Dr Achla Batra our immediate past president who had invited Dr Jyotsna Suri our guest Editor an accomplished professional with vast experience in obstetrical critical care to execute this. Dr Suri has meticulously planned and extensively edited the contents of this periodical. A galaxy of experts has contributed latest evidence-based articles on important topics including the basics and the complex conditions faced by practicing obstetricians. They have shared practical tips and new tools for monitoring, early recognition, and timely management of life-threatening conditions.

I sincerely hope that this periodical serves as a building block for all practicing obstetricians and healthcare providers towards enhancing their capacity and ability to serve our high-risk mothers and prevent the preventable mortality and morbidity.

I express my heartfelt thanks to Dr Jyotsna Suri and all contributors. Wish you all a happy reading!

Dr. Manju Puri
National President NARCHI

From the Editor-in-Chief's Desk

Dear NARCHI Members,

It is with great pleasure and pride that we present the third issue of National NARCHI Periodical. The previous two issues have been well received by all our NARCHI members. I am grateful to Dr Manju Puri, national president NARCHI for entrusting me with continued responsibility as Editor-in Chief.

This issue dedicated to 'Obstetric Critical Care', which is yet another significant aspect of maternal health is fulfilment of the idea conceived by our immediate past president, Dr Achla Batra. My sincere thanks to Dr Jyotsna Suri, Professor and unit head in VMMC and Safdarjung Hospital, for being the guest editor for this issue. She is a well-respected figure in the field of critical care in obstetrics and has been instrumental in development of this subspeciality in Safdarjung Hospital, New Delhi.

The choice of articles in this periodical is most appropriate covering all aspects of obstetric critical care and all the authors have done justice to the vision of providing evidence-based guidelines and management approaches to address the unique challenges encountered in day-to-day clinical practice.

Along with academics, we have also provided all our members with the glimpses of events held all across various NARCHI chapters.

Happy reading to all !

Prof. Monika Gupta
Professor, Obs & Gyn,
In-charge Urogynaecology subspeciality.
VMMC & Safdarjung Hospital, New Delhi

Ex- Secretary NARCHI Delhi (2018-20)

Guest Editorial

Dear Readers

Greetings of the Day!

It is with immense pleasure that I pen down this guest-editorial note for this special issue of National NARCHI periodical on Obstetric Critical Care. I am extremely grateful to Dr Manju Puri, National President, NARCHI India and Dr Achla Batra, immediate Past President NARCHI India.

The concept of obstetric critical care is now established as an essential part of maternal health services. Pregnancy is a unique physiological condition which in most cases results in a joyful outcome but in some situations can become life threatening even without warning! Even though we have made significant strides in combatting the maternal mortality and stand at 97 per lakh live births today, this progress is not seen uniformly in all parts of our country and a lot more effort is required from the health care providers to achieve the SDG Goals.

This special bulletin will sensitise our readers to important aspects of obstetric critical care- pregnancy physiological changes, early recognition, and triaging, point of care diagnosis, special investigations like ROTEM, ABG and their interpretation, use of antibiotics and pressor drugs, oxygen therapy and management of some important organ dysfunctions related to kidneys, lungs, heart and the neurological system. Special articles on managing 'Brain Dead' obstetric patient and 'brought dead' obstetric patient have also been included to clarify many dilemmas which an obstetricians may face during their practice.

I thank all the authors for contributing these articles which have been enriched by their vast experience of managing high risk pregnancies. My sincere appreciation goes out for Dr Monika Gupta as editor-in-chief for bringing this periodical into final shape.

In the end I would like to acknowledge the vision and commitment of Dr Achla Batra and Dr Manju Puri for choosing this 'Critical' topic for the National NARCHI Periodical and for entrusting their faith in me to fulfil this important task

With best wishes

Dr Jyotsna Suri

Professor, Unit Head and In-Charge Critical Care Obstetrics

VMMC & Safdarjung Hospital, New Delhi

"When we least expect it, life sets us a challenge to test our courage and willingness to change; at such a moment, there is no point in pretending that nothing has happened or in saying that we are not ready. The challenge will not wait. Life does not look back."

-**Paulo Coelho**

Impact of Physiological Changes in Management of Critical Obstetric Patients

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Introduction

Pregnancy entails a complex array of anatomical and physiological adaptations that accommodate increased metabolic demands, facilitate foetal development, and prime the body for childbirth. Distinguishing these regular physiological changes from pathological abnormalities is essential, as misinterpretation of clinical findings may result in inaccurate diagnosis and unwarranted medical interventions.

Key Physiological Changes and Their Impact on Critically Ill Patients

Cardiovascular System

The most significant cardiovascular adaptation in pregnancy is a ~50% increase in blood volume, comprising approximately 1000 mL expansion in plasma volume and a 500 mL rise in erythrocyte mass, changes that are more pronounced in multifetal gestation. This haemodilution results in physiological anaemia, which may reduce thrombosis risk by decreasing blood viscosity. Concurrently, systemic blood pressure declines, with systolic and diastolic pressures reduced by 10–15 mmHg and 20–25 mmHg, respectively, normalizing by the third trimester and contributing to widened pulse pressure (Table 1).

Cardiac output increases from 4 L/min to nearly 6 L/min due to elevated heart rate and stroke volume [CO = HR*SV]. However, beyond 20 weeks, compression of the vena cava and aorta by the gravid uterus in the supine position may transiently reduce cardiac output. Additionally, progesterone-mediated smooth muscle relaxation leads to a 20% reduction in systemic vascular resistance (SVR), starting at 5 weeks, reaching a nadir between 14–24 weeks, and gradually increasing toward term. These hemodynamic changes are critical to ensuring adequate uteroplacental blood flow throughout gestation. The normal variations in the ECG are shown in Table 2.

Table 1: Pregnancy-Induced Cardiovascular and Hemodynamic Changes

VARIABLE	CHANGE
Heart rate	Increased
Blood Pressure	Decreased
Cardiac output	Increased
Systemic vascular resistance	Decreased
Blood volume	Increased
Pulmonary vascular resistance	Decreased
PAOP	Unchanged
VARIABLE	CHANGE
CVP	Unchanged
Colloid osmotic gradient	Decreased
COC-PCOP gradient	Decreased

PAOP- Pulmonary artery occlusion pressure; **CVP-** Central venous pressure; **COP-**Colloid osmotic pressure; **PCOP-** Pulmonary capillary occlusion pressure gradient

Table 2: Normal Variations in Electrocardiogram (ECG) and Cardiac Auscultation in Pregnancy

AUSCULATION	ECG
• Apex beat in the 4th intercoastal space (Heart rotated cephalad, to the left) • Loud S1 • Ejection systolic murmur • S3 gallop	• Shortened PR and QT interval • Left axis deviation • Nonspecific ST-T wave changes • LVH

Clinical implications of changes in the CVS are:

1. Cardiac conditions like severe aortic stenosis with decreased CO or severe mitral stenosis with fixed CO may result in sudden cardiac death.
2. Pre-eclampsia associated haemoconcentration makes them more susceptible to blood loss. Moreover, due to increased vascular permeability in severe preeclampsia, vigorous intravenous resuscitation might lead to pulmonary edema.

3. In critically ill patients with sepsis, SVR may be decreased secondary to endotoxin.
4. Reduced COC and COC-PCOP predispose pregnant women to fluid overload and pulmonary edema.
5. Blood loss may be underestimated due to hypervolemia (signs and symptoms of hypovolemia may not manifest till 1500 ml of blood loss)

Hematology and Coagulation

Pregnancy induces several haematological changes to support the maternal-fetal unit. Haemoglobin decreases by ~1 g/dL, primarily due to plasma volume expansion exceeding erythrocyte mass. Relative leucocytosis is common, averaging 15,000/µL and peaking at 25,000/µL during labour, potentially mimicking infection. Platelet counts generally remain unchanged, but 5-10% of cases show gestational thrombocytopenia—a diagnosis of exclusion—necessitating differentiation from preeclampsia, autoimmune thrombocytopenia, lupus, and folate deficiency. Coagulation changes are most significant; pregnancy-induced hypercoagulability reduces postpartum haemorrhage but elevates thromboembolic risk by 4-6 times (Table 3).

Table 3: Changes in the Coagulation Factors During Pregnancy

INCREASED	UNCHANGED	DECREASED
Factor 1(Plasma fibrinogen)	Factor II	Free Protein S
Factor VII	Factor V	
Factor VIII	Factor IX	
Factor X	Protein C	
Plasminogen activator inhibitor 1	Antithrombin III	
Plasminogen activator inhibitor 2		
Von Willebrand factor		

Respiratory System

To meet the increased maternal-foetal oxygen demand, pregnancy induces several respiratory adaptations. Oxygen consumption rises by 30–50 mL/min. Minute ventilation increases from 7.5 L/min to 10 L/min, primarily due to a 40% elevation in tidal volume (Table 4, Figure 1). Arterial PCO_2 decreases from 40 mmHg to 30 mmHg, resulting in respiratory alkalosis. This is compensated by enhanced renal bicarbonate excretion, reducing serum bicarbonate from 24 mEq/L to 19–20 mEq/L. The resultant compensated respiratory alkalosis diminishes buffering capacity, increasing susceptibility to metabolic acidosis in conditions such as sepsis.

Table 4: Static Lung Volume Changes in Pregnancy

LUNG VOLUME	DEFINITION	CHANGES
Tidal volume	Volume of air inspired and expired in a normal breath	↑
Inspiratory reserve volume	Maximum volume of air that can be inspired at the end of a normal inspiration	No change
Expiratory reserve volume	Maximum volume of air that can be expired at the end of a normal expiration	↓
Inspiratory capacity	Maximum volume of air that can be inspired at the end of	↑

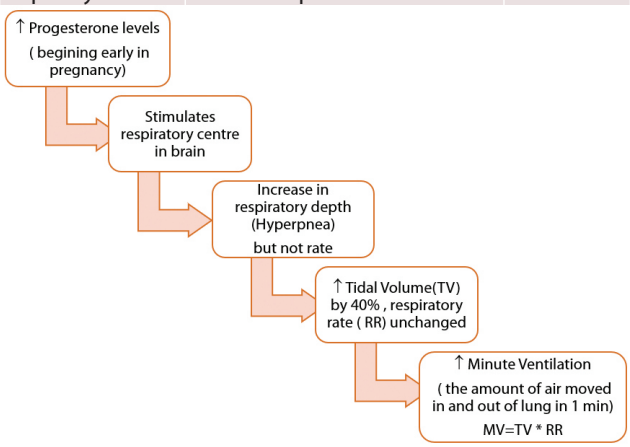

Figure 1: Physiological Changes in the Respiratory System in Pregnancy

Clinical implications of changes in the respiratory system are:

1. Due to increased oxygen consumption and decreased FRC pregnant women are more susceptible to the effects of apnoea hence, preoxygenation prior to intubation becomes necessary.
2. Considering the foetal requirement the goals of respiratory support are, PaO2 at 70 mmHg and SpO2 of 95% (vs non-pregnant value: 55mmHg and 88%)
3. The ABG analysis in pregnancy is altered, with pH more towards the alkaline side (7.40-7.46)

Renal System

Pregnancy is characterized by an increase in renal plasma flow and glomerular filtration rate (GFR) to nearly 50%, resulting in a reduced upper limit of serum creatinine (~0.8 mg/dL).

Rising progesterone promotes dilatation of the renal pelvis, calyces, and ureters starting at 8 weeks gestation, peaking in the second trimester. Additionally, uterine compression contributes to mild-to-moderate

hydronephrosis more on the right side, increasing the risk of urinary stasis and infection. Urinary protein excretion rises to 150–200 mg/day at term (vs. ~100 mg/day in non-pregnant women), with higher levels in multifetal gestation; thus proteinuria exceeding 300 mg/day requires further assessment.

Clinical implications of changes in the renal system:

1. Increased GFR leads to glucosuria, making urinalysis unreliable for diagnosing gestational diabetes.
2. In patients on phenytoin, elevated GFR and expanded plasma volume lower serum drug levels, necessitating dose adjustment.
3. Pregnancy lowers the normal serum creatinine range; even slight elevations indicate significant renal impairment.
4. Obstetric haemorrhage rapidly compromises renal perfusion, risking acute tubular necrosis, thus warranting prompt, aggressive fluid resuscitation.

Gastrointestinal and Hepatobiliary System

Pregnancy hormones notably alter gastrointestinal and hepatobiliary function. Progesterone lowers oesophageal sphincter tone, increasing reflux and aspiration risk. Estrogen and progesterone slow gastrointestinal motility and gallbladder emptying, predisposing to biliary stasis, sludge, and gallstones. Elevated alkaline phosphatase reflects placental production and is not indicative of hepatic obstruction.

Endocrine and Metabolic Changes

Several biochemical and metabolic adaptations during pregnancy are orchestrated by protein and steroid hormones.

- **Adrenal Gland**: Pregnancy induces elevated levels of total and free cortisol, aldosterone, deoxycorticosterone, corticosteroid-binding globulin, and adrenocorticotropic hormone.
- **Pancreas**: Fasting hypoglycaemia with postprandial hyperglycaemia and hyperinsulinemia is observed. Estrogen and progesterone stimulate islet cell activity, β-cell hyperplasia, and insulin secretion, enhancing peripheral insulin sensitivity. These changes increase glucose utilization, decrease gluconeogenesis, and promote glycogen storage. In late pregnancy, insulin resistance develops due to elevated progesterone, human placental lactogen, cortisol, glucagon, and prolactin, facilitating glucose transfer to the fetus. This diabetogenic state predisposes some women to gestational diabetes.
- **Pituitary Gland**: Estrogen-mediated pituitary enlargement heightens susceptibility to ischemic injury, particularly Sheehan syndrome during postpartum haemorrhage. Serum prolactin rises progressively from the first trimester, reaching tenfold elevations by term.
- **Thyroid Gland**: Although pregnancy is overall euthyroid, significant hormonal fluctuations occur:
  1. Enhanced renal iodine clearance creates a relative iodine-deficient state, increasing maternal and fetal hypothyroidism risk.
  2. Estrogen-induced rise in thyroxine-binding globulin elevates total T3 and T4, though free T4 remains stable.
  3. First-trimester hCG-mediated TSH suppression is transient, normalizing by the end of the first trimester.
  4. Postpartum, heightened thyroid autoantibody levels elevate the risk of postpartum thyroiditis and exacerbate pre-existing Graves' disease.

Immunology

There are various foetal mechanisms like alteration in major histocompatibility complex class 1 expression as well as maternal factors such as uterine natural killer cells and shift of the T helper cell profile from Th type1 to Th type 2, this immunological adaptation at the maternal-foetal interface prevents foetal rejection. This mechanism might also explain the increased susceptibility of pregnant women to viral infections.

Physiological changes in pregnancy often obscure early signs of critical illness, complicating timely diagnosis and management. There are various obstetric and non-obstetric causes of maternal critical illness and tailored scoring systems designed to account for these physiological alterations, ensuring appropriate intervention.

Obstetric critical care is defined as "the specialized management of critically ill obstetric patients via an interdisciplinary approach in which the optimization of the clinical variables of pregnant women should be approximated to the maternal-fetal unit needs as a whole".

Altered Physiology- Unique Scoring Systems for Assessing Critically Ill Obstetric Patients:

Since standard ICU scoring methods may inadequately categorize the patients due to various physiological changes in pregnancy, modified tools have been devised to assess critically ill patients for appropriate and timely management.

1. **OEWS** (Obstetric Early Warning Score): Integrates

various parameters for early detection of worsening of preeclampsia, hemorrhage and sepsis.

- Heart Rate
- Blood pressure
- Urine output
- Proteinuria
- Altered consciousness

2. **Obsterically Modified qSOFA score:** Quick sepsis-related organ failure assessment

   A quick bedside assessment tool to identify patients at high risk for poor outcomes.

   It has 3 components, with a score of 0 to 3 for the following clinical signs:
   1) Systolic blood pressure < 90mmHg
   2) Respiratory Rate > 25/ min
   3) Altered mentation

3. **Obstetrically modified SOFA Score:** In this score, the triggers of serum creatinne and neurological evaluation were modified as compared to the original SOFA score

Conclusion

The physiological adaptations of pregnancy encompass nearly all organ systems and warrant meticulous consideration in the management of critically ill patients. Misinterpretation of these gestational alterations as pathological findings may precipitate diagnostic inaccuracies, therapeutic misjudgements, and adverse clinical outcomes.

Key Points

- Physiological changes in pregnancy are protective for the gravid woman and her developing fetus
- However these changes have to be understood by the treating obstetrician and critical care physician while managing a pregnant woman with critical illness
- The CVS changes make a woman with stenotic heart lesions more susceptible to failure in pregnancy
- The changes in the hematopoietic system increases susceptibility of an obstetric patient to thromboembolic disease
- The increase in tidal volume changes the normal values of the Arterial Blood Gases and its interpretation
- The decrease in functional residual capacity makes a pregnant woman very susceptible to any hypoxic insult
- Changes in immunological system make a gravida more prone to serious viral infections

Suggested Reading

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Recognition of Deteriorating Obstetric Patient- Role of Early Warning Scores

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Introduction

A deteriorating obstetric patient is a pregnant individual whose medical condition is worsening, potentially posing significant risks to both the mother and foetus. Signs of deterioration may include increasing pain, abnormal vital signs, severe bleeding, or signs of infection.

Prompt assessment and intervention are critical to prevent maternal morbidity and mortality. The application of physiological parameter-based screening tools at admission in labour room is one strategy to prevent maternal morbidity and mortality in healthcare settings.

The key elements that can help in reducing the likelihood of adverse obstetric events are:

- Understanding how pregnancy alters normal physiological measures and how these affect the pregnant patient's evaluation. Many conditions are masked due to physiological changes.
- To comprehend how the modified early warning score for obstetrics (MEOWS) is used to monitor individuals who are at risk of deteriorating.
- Knowing when to use "SBAR" to escalate (S- situation, B – background , A- assessment, R – recommendation)
- To identify obstetric "red flag" symptoms
- The caregiver must be aware of the patient's immediate care needs

Early warning scores (EWS) in a patient with a deteriorating clinical condition is a standardized scoring system that monitors vital physiological signs such as temperature, heart rate, blood pressure, and respiratory rate which helps for early recognition of a worsening clinical condition and timely treatment.

Modified Early Obstetric Warning Score (MEOWS)

The Confidential Enquiry into Maternal and Child Health (CEMACH) recommends the Modified Early Obstetric Warning Scoring System(MEOWS) as a crucial step to be applied to all obstetric admissions.

1. MEOWS must be utilized for all pregnant patients right from the time of positive pregnancy test until 42 days after delivery.
2. Measurement and observations of parameters should be done by staff members who have received the necessary training to do so.
3. Every observation should be documented clearly and the date and time should be mentioned.

Important Parameters

Heart rate – A woman with tachycardia should be considered hypovolemic until proven otherwise.

Temperature - Temperature changes (both rise and fall) indicate sepsis, therefore a workup and antibiotic treatment have to have started right away.

Blood Pressure- Hypotension indicates decompensation and is a late indicator. Pregnancy and delivery-related physiological changes can make it challenging to identify.

Oxygen saturation-The oxygen administration rate (L/min) must be recorded beneath the saturations. If a woman needs oxygen to keep her saturation within the usual range, the MEOWS score should be increased by two.

Neuro response:

AVPU is a measure of consciousness.

The following are the best responses:

A – Alert and conscious.

V – Responds to verbal stimulus

P – Responds to painful stimulus only

U – Unresponsive to any form of stimulus

An AVPU score decline should always be regarded as significant.

1. MEOWS Score Chart

Physiological Parameters	3	2	1	0	1	2	3
Respiratory rate		<8		9-20	21-25	26-30	>30
O2 Saturation	<90	90-93	94-95	>96			
Supplementary O2 Device		YES		NO			
Temperature		≤35 C	35.1-36.0	36.1 - 37.4	37.5-38.0	38.1-39	≥39.1
Systolic BP	<80	80-89	90-99	100 - 140	141-160	161-170	>170
Diastolic BP		≤40		41-89	90-99	100-110	>110
Heart rate	<40	40-50	51-59	60-100	101-110	111-120	>120
Levels of consciousness				A	V	P	U/NC
Urine Output	<10 ml/hr	<50 ml/2hrs	<100 ml/4 hr	≥100 ml/4 hr			

MEOWS Observation and Escalation Chart

Table 1: MEOWS Chart and Escalation Protocol

MEOWS SCORE	RISK	FREQUENCY OF OBSERVATIONS	ESCALATION PROTOCOL
0	LOW	Minimum of 12 Hrly Minimum of 8 hrly Minimum of 4 hrly	
1	LOW	Repeat MEOWS IN 1 hour	Inform shift in-charge if continues to score after 1 hour, Document plan of care
2-3	LOW	Recheck MEOWS in 1 hour	Inform Shift charge And 1st on call. Make a plan of management Record action in case notes.
4-6	MEDIUM	Repeat MEOWS in 30 minutes	Inform the Shift leader and 2nd on-call obstetrician to attend within 1 hour of receiving the call. Make a plan of management. Record action in case notes
7 or above	HIGH	Repeat observations every 15 minutes	Discuss the case with the consultant obstetrician and consultant anaesthetist to attend the ward within 15 minutes of receiving the call. Make a plan of management. Record action in case files

Many studies have found MEOWS to be feasible and acceptable, and have suggested that the recording of vital signs improved with the implementation of MEOWS .

Red Flag Signs in Obstetrics are shown below (Figure 1).

Pyrexia
Fever >38 C
PR>100/min
RR>20 /min
Abdominal/chest pain
Diarrhoea/vomiting
Decreased fetal movement
Spontaneous Rupture of membrane/ Significant Vaginal diacharge
Uterine/Renal angle tenderness

Breathlessness
Sudden onset
Associated with chest pain
Orthopnoea,
paroxysmal nocturnal dyspnoea
New onset wheeze

Headache
Sudden onset
Associated neck stiffness
Worst headache ever
Any neurological sign

Abdominal Pain & Diarrhoea
Sudden onset Fainting and dizziness
Severe pain without an established cause
Need to consider non-obstetric causes

Anxiety & Distress
Known psychiatric history
Marked change in symptoms from normal function
Are the only psychological signs behavioral & non specific e.g. distress agitation

Figure 1: Red Flags in Obstetrics

The steps of rapid response to red flags:

- Call for senior help
- Increase observation frequency
- Monitor pulse oximetry +/- O2
- Make the patient take a left lateral tilt or make her sit up
- Start CTG tracing if the patient is antenatal
- Start IV lines
- Administer necessary medications oral or parenteral
- Get quick lab results
- Do ECG if indicated
- Do ABG (Arterial blood gas analysis)
- Inform family and maintain notes and document

The suggested flow chart for the EWS intervention is shown below (Figure 2).

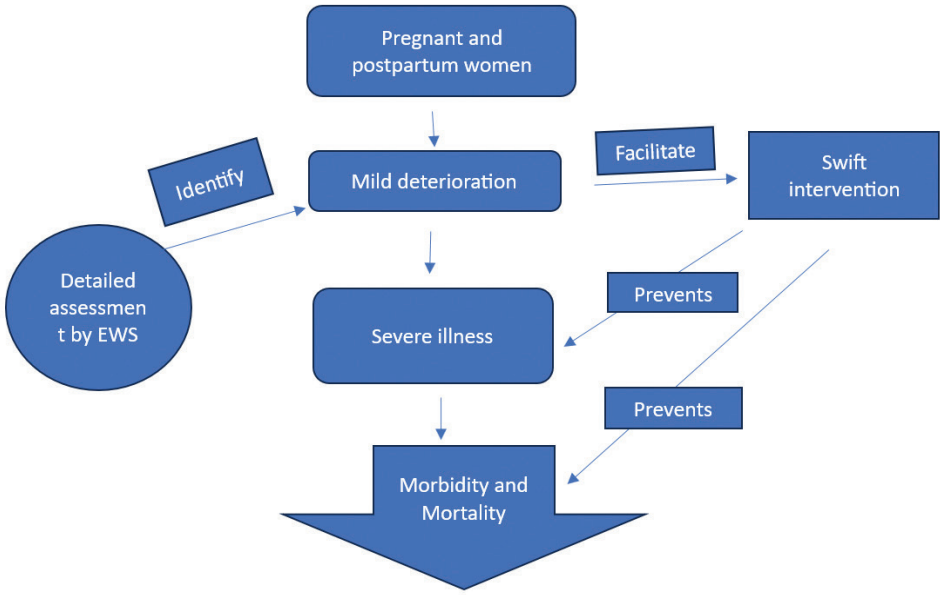

Figure 2: Flow Chart for the EWS Intervention

2. CART (Cardiac Arrest Risk Triage) Score

This score predicts risk of in-hospital cardiac arrest (Table 2).

Parameters	Range of variables	Score
Respiratory rate/min	<21 21-23 24-25 26-29 >29	0 +8 +12 +15 +22
Heart rate, beats/ min	<110 110-139 >139	0 +4 +13
Diastolic BP, mmHg	>49 40-49 35-39 <35	0 +4 +6 +13
Age, years	<55 55-69 >69	0 +4 +9

Interpretation:

Table 2: CART (Cardiac Arrest Risk Triage) Score

	CART Score	Risk of cardiac arrest within 48 hours
1	≤20	Low
2	>20	High

Scores > 20 were 90 % specific in the validation study by Chuprek et al and 91.9% specific in the original study for the prediction of cardiac arrest within 48 hours.

Electronic cardiac arrest triage score is a mode using 33 variables which includes vital parameters and laboratory data. While many studies have validated this score in post-operative patients and are said to be most accurate.

3. APACHE II Score (Acute Physiology and Chronic Health Evaluation II)

Apache score is determined using 12 physiological variables at the end of the first 24 hours of ICU admission.

Total APACHE Score =Sum of Age points(AP)+Chronic Health Points(CHP)+Acute physiological score(APS)

Table 3: Scoring vs Predicted risk of Mortality Incidence

Score	Mortality
0-4	4%
5-9	4%
10-14	15%
15-19	25%
20-24	40%
25-29	55%
30-34	75%
>34	85%

Structured reviews however have shown that mortality risks are consistently overestimated by APACHE II score in obstetric patients.

4. Carle's Obstetric Warning Score (Carle's OEWS):

A statistically based design clinically modified obstetric early warning score. Carles OEWS stands apart from the rest of the scores as it is statistically derived, clinically modified, and internally validated. Also, varied regional versions with varied cutoffs from parameters are available.

Table 4: Carle's Obstetric Warning Score (Carle's OEWS)

	Clinical parameters	OEWS 3	4	OEWS1	Normal	OEWS1	OEWS2	OEWS3
1	SBP (mmHg)	<80	80-89		90-139	140-149	150-159	≥160
2	DBP(mm Hg)				<90	90-99	100-109	≥110
3	RR(/min)	<10			10-17	18-24	25-29	≥30
4	HR(/min)	<60			60-110		111-140	≥150
5	O2 required to maintain SpO2 ≥96 %				None(Room air)	24-39		≥40
6	Temp(C)	<34		34-35	35.1-37.9	38-38.9		≥39
7	Conscious level				Alert			Non -alert

5. Obstetrically modified SOFA (Sequential Organ Failure) Score:

SOFA is a validated scoring system that remains accurate when applied to patients with sepsis and with evidence of hypoperfusion. SOFA score is a simple and objective score that allows an aggregate measure of the severity of organ dysfunction among 6 major organs and helps in the prediction of mortality risk.

Table 5: Obstetrically modified SOFA (Sequential Organ Failure) Score

	SOFA score	1	2	3	4
1	Respiration				
	Pao2/FiO@(mmHg)	<400	<300	<220	<100
	SaO2/FiO2	221-301	142-220	67-141	<67
2	Platelets(10 3/mm3)	<150	<100	<50	<20
3	Liver Bilirubin(mg/dL)	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
4	Cardiovascular				Dopamine>15
	Hypotension	MAP<70	Dopamine≤5 or dobutamine(any)	Dopamine>5 or norepinephrine ≤0.01	Or norepinephrine>0.1
5	CNS				
	Glasgow coma scale	13-14	10-12	6-9	<6
6	Renal Creatinine(mg/dL) or urine output(mL/day)	1.2-1.9	2.0-3.4	3.5-4.9 Or <500 ml/day	>5.0 or <200ml/day

6. Maternal Early Warning criteria: The Maternal early warning criteria have been drawn from MEOWS Red Triggers. Patients who have any triggers should receive immediate evaluation by the clinician and immediate therapeutic interventions (Table 6).

Table 6: Maternal Early Warning Criteria

1	Systolic BP(mm Hg)	<90 or >160
2	Diastolic BP (mmHg)	>100
3	Heart Rate(beats per min)	<50 or >120
4	Respiratory rate(breaths per minute)	<10 or >30
5	Oxygen saturation on room air, sea level %	<95
6	Oliguria, ml/hr for ≥2 hours	<35
7	Maternal agitation, confusion, or unresponsiveness, Patient with preeclampsia, reporting a non-remitting headache or shortness of breath	

In a systematic review of Early warning scores in obstetric patients had shown the Sensitivity of early warning scores to be 89% and specificity-85%. Obstetric EWS has high accuracy over the prediction of deaths among critically ill obstetric patients(area under receiver operator curve>0.80.

For the obstetric population admitted to the critical care unit, early warning systems created using a statistically determined model are accurate in predicting death (AUROC >0.80) . With a somewhat low PPV (average of 41%), EWS has been demonstrated to be very sensitive and specific in predicting morbidity and ICU admission in various general obstetric populations. Khergade et al in a recent cohort study have shown that Obstetric early warning scores are as effective as SOFA and APACHE II scores to prognosticate the obstetric pateints. Although APACHE II and SOFA scores are excellent predictors of maternal mortality but they need certain laboratory parameters and which take 6-8 hours, and so prognostication directly at admission is not possible.

Conclusion

The use of Early Obstetric Warning Scores (EOWS) in critical care obstetrics has proven to be an invaluable tool in enhancing maternal safety and outcomes. By providing a systematic approach to the early detection of physiological deterioration, EOWS empowers healthcare providers to respond swiftly and effectively to the onset of life-threatening conditions such as severe preeclampsia, sepsis, and postpartum hemorrhage. The integration of these scores into clinical practice fosters a culture of vigilance and timely intervention, ultimately improving maternal morbidity and mortality rates.

Case scenario

Mrs. A 26-year-old Primigravida at 39 weeks of gestation was admitted to the labour room with mild sustained pain abdomen, feeling of dizziness, and swelling in her legs.

- General Appearance: Pale, mild oedema in both lower legs, and appears anxious.
- Vital Signs:
  - o Blood pressure:145/90 mmHg (Elevated compared to baseline)
  - o Heart Rate: 110 bpm (Tachycardic)
  - o Respiratory Rate: 18 breaths/min (Normal)
  - o Temperature: 37.8°C (Mildly elevated)
  - o Oxygen Saturation: 97% on room air (Normal)
- Physical Examination:
  - o Abdomen: Tenderness noted on palpation of the lower abdomen, no signs of rigidity or guarding.
  - o Urine Output: 150 mL over the last 4 hours (Normal output but on the lower end for the patient's condition).

Modified Early Obstetric Warning Score (MEOWS) Calculation for the Case:

Parameter	Normal Range	Score
Blood Pressure (mmHg)	<140/90	2 (Elevated)
Heart Rate (bpm)	60–100	2 (Tachycardic)
Temperature (°C)	36–37.5	1 (Mildly elevated)
Respiratory Rate (breaths/min)	12–20	0 (Normal)
Oxygen Saturation (%)	95–100	0 (Normal)
Urine Output (mL/4hrs)	>200	0 (Normal)

- Total MEOWS Score: 5

Clinical Interpretation: MEOWS of 5 indicates a moderate concern for a deteriorating obstetric condition. This score suggests that the patient is at risk for developing a serious complication and requires close monitoring and possible intervention.

Key points

- Physiology in the mother markedly changes during pregnancy to compensate increased demands of fetus. Hence making early detection of deteriorating clinical status even more difficult.
- An Obstetric early warning score should be used in all women to allow early recognition of women becoming critically ill.
- Use of EWS helps in a systematic approach to management.
- Till now Carles OEWS has been found the best

statistically designed score

- Obstetric early warning score to be used in conjunction with clinical judgment.

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Recurrent Seizures in Pregnancy- Differential Diagnosis and Management

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Introduction

Peripartum seizure represents a critical obstetrical emergency, posing significant risks of morbidity and mortality to both the mother and fetus. Seizures during pregnancy complicate 0.1% of all gestations. The differential diagnosis of seizures in pregnancy is extensive. Determining the underlying etiology is crucial in the management of these patients. The most frequent cause is eclampsia. Other than eclampsia, a host of conditions may give rise to seizures during pregnancy and must be actively sought. These include underlying epilepsy, stroke, CVST (central venous sinus thrombosis), PRES (posterior reversible encephalopathy), metabolic derangement, CNS (central nervous system)infections such as meningitis and encephalitis, autoimmune encephalitis, CNS space occupying lesions. In patients with epilepsy, low antiseizure medication drug levels are also an important cause.

Recurrent seizures during pregnancy are highly dangerous for both the mother and the fetus. Tonic-clonic seizures, in particular, can lead to severe complications:

- **For the mother:** Physical injuries, placental abruption (which disrupts the connection between the placenta and uterus), and aspiration, potentially resulting in aspiration pneumonitis.
- **For the fetus:** Hypoxia (lack of oxygen), acidosis, intracranial hemorrhage, and, tragically, even fetal death in extreme cases.

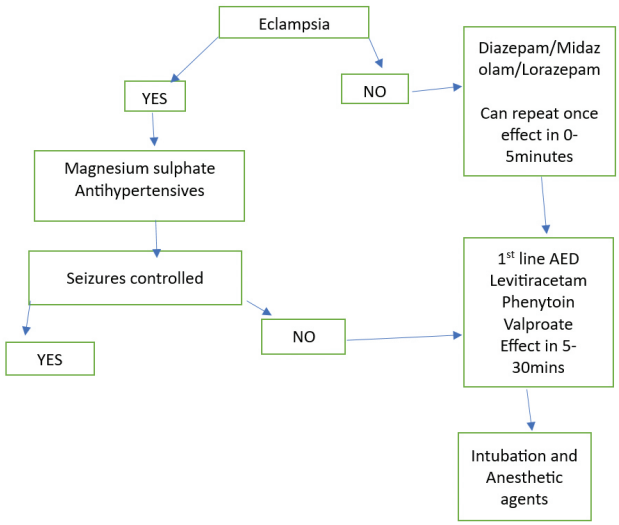
Acute management of seizures during pregnancy is critical for safeguarding both the mother and fetus. The immediate steps include:

- ABC (airway, breathing, circulation); give O2 During the convulsive episode, hypoventilation and respiratory acidosis often occur. Although the initial seizure lasts only a few minutes, it is important to maintain oxygenation by supplemental oxygen administration via a face mask with or without oxygen reservoir at 8–10 L/min.
- Left lateral decubitus position after seizure subside.
- Elevate bed railing, put in a padded tongue blade to prevent tongue bite.
- Obtain IV access and simultaneously do blood glucose by glucometer.
- Catheterize the patient and do urine albumin.

Further management involves identifying the underlying cause of the seizure and initiating appropriate treatment, such as administering magnesium sulfate for eclampsia or addressing other triggers like hypoglycemia. Continuous fetal monitoring is also vital during this period.

Eclampsia is kept as first diagnosis in 2nd half of pregnancy. A quick history should be taken to rule out other causes. The drug of choice for eclampsia is magsulphate, if not controlled by magsulphate then other drugs should be considered. Prevention of recurrence is of utmost importance, if seizures are not controlled by initial dose of magsulphate, then a repeat dose of 2gm is given and if still recur than 2nd line drug is levetiracetam or phenytoin. If seizures are still not controlled, then patients need to be intubated as shown in the algorithm below.

Algorithm for Management of Seizures in Obstetric Patient



If blood pressure is high systolic, ≥160mm of Hg or diastolic ≥110mm Hg, then emergent antihypertensive agents for acute management of blood pressure have to be given.

Patient has to be monitored for magnesium toxicity

by knee jerk, respiratory rate every 15 minutes and urine output hourly. Biochemistry for other organ involvement -urea, creatinine, LFT, haemogram, platelet count and LDH are done. Blood glucose is an essential investigation in such women as the seizures may also occur because of hypoglycemia. This is rapidly reversible with 50 ml of 50% dextrose solution plus100 mg thiamine.

If the cause of seizures is not eclampsia, then the first line drugs to be given are summarized in Table 1

Table 1: Doses and Side Effect Profile of Anti-Seizure

Medications

Drug	Loading Dose	Maintenance Dose	Side Effects
First line agents			
Lorazepam	0.1 mg/kg, up to 4 mg IV at 2 mg/min upto10mg	Repeat loading dose once if needed	Sedation, respiratory depression hypotension, arrhythmia
Midazolam	0.2 mg/kg, up to 10 mg IV / IM / Intranasal / Buccal	Repeat loading dose once if needed	Sedation, respiratory depression, hypotension
Diazepam	0.1 mg/kg, up to 10 mg IV or 0.2 mg/kg, up to 20 mg rectally	Repeat loading dose once if needed	Sedation, respiratory depression, hypotension
Second line agents			
Levetiracetam	100 0mg I/v over 15min up to 500 mg/min Dilute to 100cc for infusion	500mg I/V bd.	Mild sedation, psychosis, behavioral and mood changes * No cardiovascular reactions.
Phenytoin	18-20 mg/kg IV, up to 50 mg/min)	5-7 mg/kg/day orally / IV, divided every 8 hrs.	Hypotension, sedation, ataxia, cardiorespiratory depression, arrhythmia, infusion site injury, purple glove syndrome *Enzyme inducer
Third line agents			
Ketamine	1.5 mg/kg IV every 5 min until seizures controlled or maximum dose 4.5 mg/kg	1.2-7.5 mg/kg/hr, continuous IV	Hypertension, raised intracranial pressure
Etomidate	0.3 mg/kg IV every 5 min, until seizures controlled	1.2-7.2 mg/kg/hr, continuous IV	Hypotension, adrenal insufficiency, myoclonus
Lidocaine	1-5 mg/kg (usually 100 mg) IV every 5 min until seizures controlled	Up to 6 mg/kg/hr, continuous IV	Cardiac arrhythmias
Midazolam	0.2 mg/kg IV; repeat 0.2–0.4 mg/kg boluses every 5mins until seizures stop, up to a max total loading dose of 2mg/kg	Loading dose: 0.1 mg/kg/h Continuous infusion rate: 0.05–2 mg/kg/h.	Hypotension, sedation, cardiorespiratory depression
Propofol	1–2 mg/kg IV; repeat 1–2 mg/kg boluses every 3–5 mins until seizures stop, up to max total loading dose of 10mg/kg	Loading dose: 2 mg/kg/hr Continuous infusion rate: 1–15 mg/kg/hr	Hypotension, propofol infusion syndrome
Pentobarbital	5mg/kg iv upto 50 mg/min; repeat 5 mg/kg boluses until seizures stop	Loading dose: 1 mg/kg/hr Continuous infusion: 0.5–10 mg/kg/hr	Hypotension, sedation, ataxia, cardiorespiratory depression

The patient has to be closely monitored with pulse, BP, respiratory rate, consciousness level (GCS) and oxygen saturation.

Fetal Monitoring

Maternal seizure activity is associated with uterine hypertonus and fetal bradycardia. Continuous fetal heart rate monitoring is essential, particularly when the fetus is at a viable gestational age. During or shortly after seizures, fetal heart tracing abnormalities are commonly observed. Maternal hypoxemia may result in:

- Loss of variability and a category II fetal tracing.
- Prolonged hypoxemia leading to fetal bradycardia and a category III fetal tracing, which generally resolves within 3–10 minutes when maternal oxygenation improves through treatment, prevention of seizures, positioning, and supplemental oxygen.
- The presence of fetal tachycardia, absent variability, or a sinusoidal pattern may indicate placental abruption and fetal anemia and immediate delivery is warranted.

Diagnosis of Etiology of Non-Eclamptic Seizures

The first diagnosis in case of seizures in pregnancy is eclampsia. In case seizures do not respond to magsulf therapy or other localising neurological signs are present then other diagnosis should be considered

Although not always feasible, a detailed description of the event is helpful in both classifying the event as a seizure and to rule out differential diagnoses. This description includes possible triggers, behaviours, and postictal symptoms, if present. Attempts should also be made to uncover past episodes and underlying risk factors such as medications, poisonings, medical comorbidities, or genetic predispositions.

To establish etiology, EEG, CT Scan Head / MRI brain, metabolic profile, biochemistry and if required CSF analysis (if CNS infection is suspected).

EEG- if no other cause suspected EEG is the initial test. EEG is safe during pregnancy Approximately 50% of the time, patients who are clinically diagnosed with seizures have normal EEGs. Thus it is important to remember that a normal EEG does not rule out the diagnosis of a seizure disorder. On the other hand, abnormalities found on EEG can predict the risk for seizure recurrence as well as they help to guide therapy.

Imaging -CT of the head delivers 01 rad to the fetus which is safe for the fetus. According to the American College of Radiology, no single diagnostic X-ray procedure results in radiation exposure to a degree that would threaten the well-being of the developing preembryo, embryo, or fetus. MRI is more sensitive than CT in detecting subtle lesions and there is no exposure to ionizing radiation but, CT scans are often used because they are quicker and more readily available in an acute situation. Imaging can diagnose a space occupying lesion and also differentiate between PRES, CVST and stroke.

Obstetric Management

Delivery may be required at any gestational age in cases of eclampsia. However, immediate cesarean delivery is not always mandatory, even in the presence of fetal bradycardia. Prior to delivery, efforts should focus on stabilization through anticonvulsants, oxygen supplementation, antihypertensives, uterotonics, and maternal repositioning. Transporting an actively seizing patient to the operating room without stabilization can worsen outcomes. Only if Category III Fetal Heart Tracing is persistent despite 10–15 minutes of resuscitative may signal placental abruption, warranting immediate delivery.

If the cause of seizures is not induced by pregnancy then decisions of delivery should be individualized based on maternal and fetal status and consultation with neurologist or neuro surgeon Coordination with the neonatal care team is essential, considering the potential for neonatal CNS depression from administered benzodiazepines and other anti-epileptic drugs.

Conclusion

Recurrent seizures during the peripartum period can result from various pathologic conditions, some of

which are life-threatening. While eclampsia should be the primary consideration, other potential causes must be evaluated as differential diagnoses. Given the non-specific nature of clinical symptoms, neuro-imaging plays a pivotal role in guiding the diagnostic process. Since many underlying causes of seizures in this period tend to overlap, effective diagnosis and management should involve a multidisciplinary approach to ensure comprehensive care and tailored treatment plans.

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Approach Towards Acute Dyspnoea in Pregnant and Postpartum Patient

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Introduction

Dyspnoea is defined by the American Thoracic Society as "Subjective experience of breathing difficulty that is comprised of qualitatively distinct sensations that vary in intensity".

Knowledge of the physiological changes in respiratory system in pregnancy is essential to differentiate normal findings from pathological changes.

Some of the key physiological changes in the respiratory system in pregnancy are :

- Increased Minute ventilation
- Decreased FRC & ERV
- Increased CO2 washout → Physiological respiratory alkalosis
- pH between 7.40 t0 7.47
- PaO2- 101-105 mmHg
- PaCO2 27-32mmHg

Physiological Dyspnoea

Hyperventilation is a normal physiological process in pregnancy caused by increased depth of respiration induced by hormones progesterone and oestrogen. Many factors acting together result in hyperventilation like the increase wakefulness drive to breathe , increase in central and peripheral chemoreceptor sensitivity , reduction in the ventilator recruitment threshold and increase in metabolism.

The respiratory cycle consists of a forward part (respiratory muscles), and a feedback part (chemoreceptors dependent response to the PaO_2, PCO2 and hydrogen ions in the blood)

Dyspnoea results from a mismatch between the feed-forward message to the ventilatory muscles and a heightened feedback from chemoreceptors monitoring the response to decrease in $PaCO_2$ levels.

Physiological dyspnoea begins during early pregnancy and gradually progresses, is not accompanied by any other symptoms or signs like chest pain, cough, expectoration, rhonchi , crepitations or hypoxemia and has no abnormal findings on investigations.

The common pathological causes of acute dyspnoea in a pregnant woman and the approach towards such a patient are shown in Table 2 and 3

Table 1: Common Pathological Causes of Acute Dyspnoea

Pulmonary causes	**Cardiac Causes**	**Obstetric Causes**	Others
Bacterial Pneumonia	Rheumatic valvular Heart Disease	Preeclampsia with pulmonary oedema	Anaemia
Tuberculosis	Congenital heart disease	Pulmonary embolism	Sepsis
Viral pneumonia-Covid 19 , HINI, Influenza	Ischemic heart disease	Amniotic fluid embolism	Diabetic keto-acidosis
Asthma	Arrythmias	Obstetric sepsis	Thyrotoxicosis
Pleural effusion	Cardiomyopathy	Obstetric Haemorrhage causing ARDS	Ascites
Pneumonitis		TRALI	Uraemia
Pneumothorax		Polyhydramnios	Trauma
ARDS		Drug related -Tocolytic, oxytocin	Anaphylaxis
		Fluid overload	
		GTN	

Table 2: Approach to a patient with acute onset dyspnoea

History	Examination
• Quick and detailed history from patient/attendant • Onset, duration, progression, severity, seasonal and diurnal variation • Associated symptoms like fever, cough, sore throat, wheeze, chest pain, palpitations, dizziness syncope, haemoptysis, loose stools, vomiting, pain abdomen, prolonged immobilization • History of similar episodes in past • Obstetric complications -Preeclampsia, haemorrhage, polyhydramnios, GTN, delivery complications • Medical disorders -Heart Disease, diabetes, hypertension, thyrotoxicosis ,DVT, drug allergy, Treatment received • Surgical history : Prior surgery including caesarean section, recent surgery • Family history : Thromboembolism, heart disease	• General Physical Examination • Mentation, hydration, temperature • Respiratory rate, SpO2, • Pulse rate /volume/synchronicity /BP • Pallor/Icterus,/Cyanosis,/Clubbing/Lymphadenopathy/ Pedal oedema, Generalized anasarca • Neck examination: JVP, thyromegaly, prominent pulsations, • Respiratory System: Any added sounds: crepitations, rhonchi, diminished or absent air entry, bronchial breath sounds • Cardiovascular system: S1, S2, any added sounds, murmur, thrill, precordial pulsations. • Central nervous system: sensory and motor functions, spinal deformity • Per abdomen: hepatosplenomegaly, obstetric examination • Per speculum and per vaginal examination if indicated

Initial management : Propped up position/oxygen therapy and investigations for cause of breathlessness (Table 3).

Table 3: Investigations for an acutely dyspnoeic patient

- Arterial Blood Gas (ABG)
- Bedside chest X ray and ECG
- Check spot glucose by glucometer
- Complete blood count with peripheral smear
- Random blood sugar,
- Coagulation profile, D-dimer,
- Liver function test, Kidney function test, Serum Electrolytes,
- Imaging modalities in emergency department are pivotal for fast triage
  - ➢ Point of care Ultrasound: (POCUS)
  - ➢ Bedside lung ultrasound in emergency (BLUE protocol,
  - ➢ Bedside cardiac ultrasound,
    - ✓ Compression ultrasound of legs in suspected pulmonary embolism
    - ✓ Other Imaging modalities :
- Complete Echocardiography if required
- CT Pulmonary angiography (CTPA) or Ventilation Perfusion scan
- CT Lung
- Other investigations as and when required:
- Nasopharyngeal swab for RTPCR for Covid 19
- Sputum for AFB smear and culture
- Sputum for bacterial culture
- Serum procalcitonin
- Urine routine microscopy and culture sensitivity
- Natriuretic peptides-proBNP/BNP, troponins
- Add investigations as per the provisional diagnosis

Role of Point of Care Ultrasound in a Dyspnoeic Patient

Bed side lung examination in emergency (BLUE protocol)

A linear transducer is used for visualizing the pleura.

Phased array or curvilinear transducer is used for lung examination. The probe is placed in the intercostal space in vertical orientation to the ribs with an imaging depth of around 18 cm to visualize the entire lung parenchyma from anterior to posterior. In the normal lung, the pleura appears as a horizontal hyperechoic sliding line below which horizontally oriented reverberation artifacts called A-lines are seen which are equidistant from each other (Figure 1). These artifacts are caused by ultrasound beam striking the air in the alveoli.

In pulmonary oedema vertical reverberation artefacts called B-lines appear due increased density of lungs caused by fluid (Figure 2). These are laser-like vertical hyperechoic lines that start at the pleural line and extend to the bottom of the screen without fading and move synchronously with lung sliding.

In consolidation, the lung appears like the liver called hepatization of lung tissue caused by secondary collapse following reduced aeration.

A thickened irregular pleural line suggests infection of pleura whereas pleural effusion appears as anechoic

fluid when it is transudate or hypoechoic fluid in exudate.

Pneumothorax is diagnosed by "lung point" sign which is the absence of pleural sliding cause by separation of visceral and parietal pleura due to accumulation of air in the pleural space.

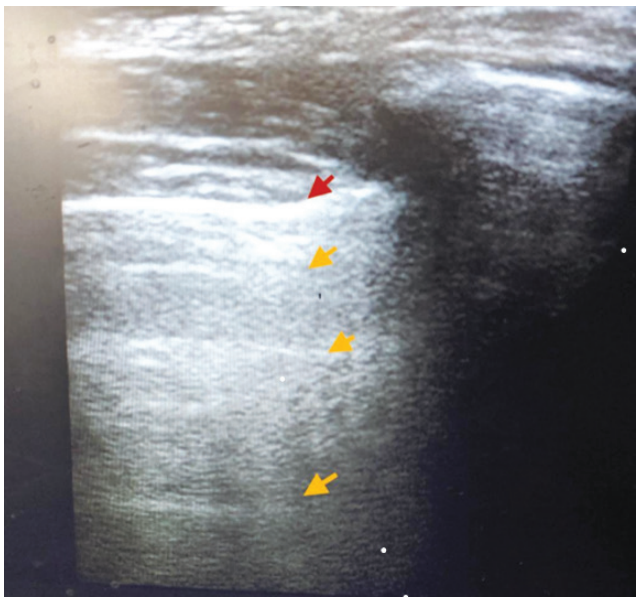


Fig 1: Normal Lung Scan: Pleura (red arrow) A lines (yellow arrow)

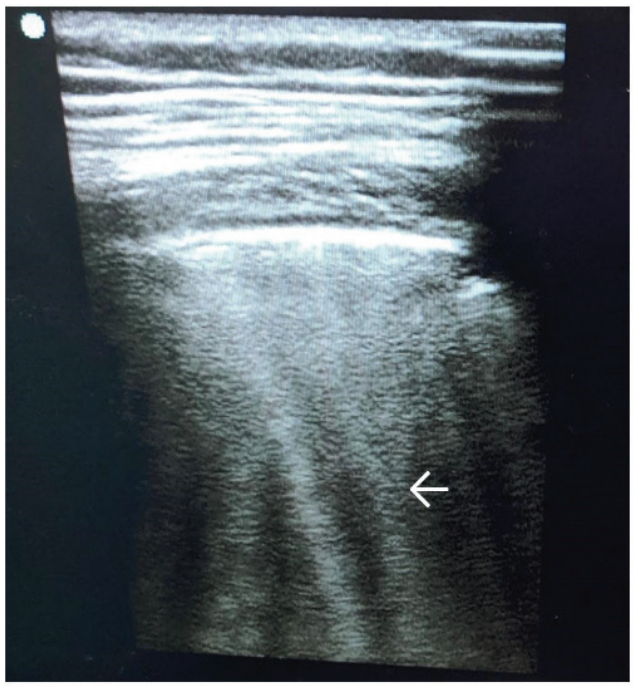


Fig 2: B Lines (white arrow) in Pulmonary Edema

Evaluation of heart : FoCUS (focused cardiac ultrasound)

The basic cardiac ultrasound can be learnt even by clinicians who are not trained to perform comprehensive echocardiography. FoCUS is aimed to detect pericardial effusion/cardiac tamponade, left and right ventricular size and function, intravascular volume status, and may aid decision-making during cardiopulmonary resuscitation.

The following 5 views are to be obtained: Long parasternal view, short parasternal view, 4 chamber apical view, 4 chamber subcostal/subxiphoid view and subcostal IVC view (Figure 4-8)

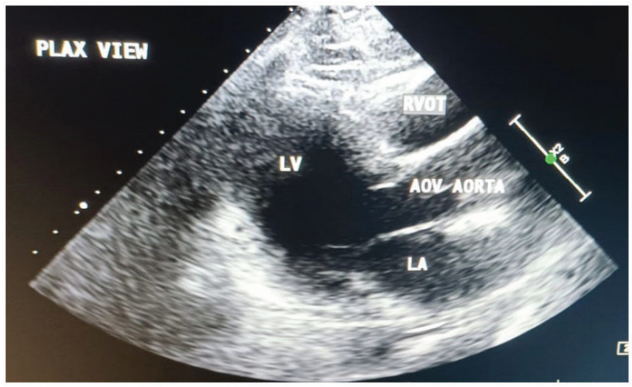


Fig 4: Parasternal long axis view (PLAX)

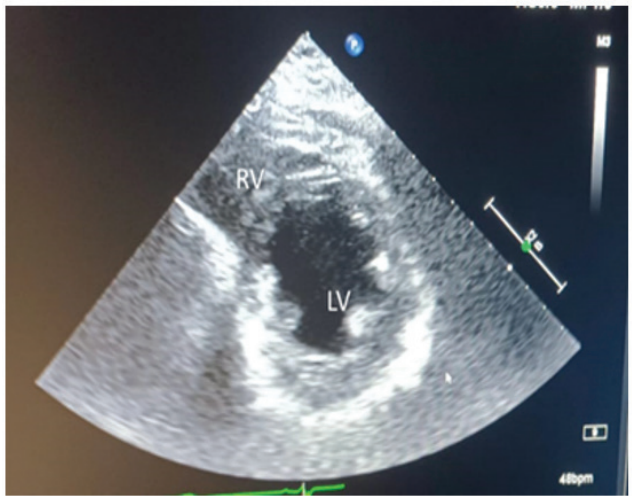


Fig 5: Short parasternal View (SPAX)

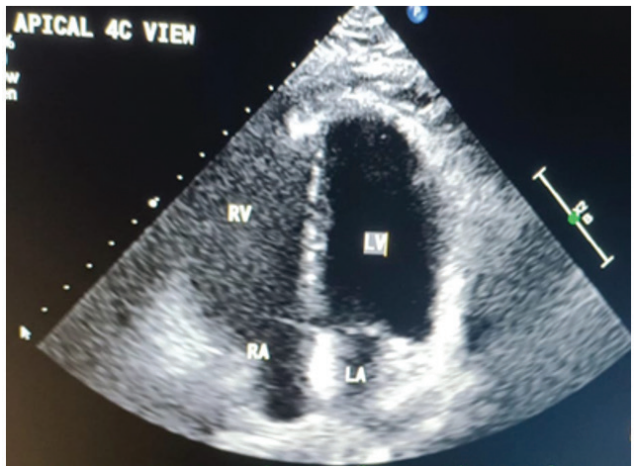


Fig 6: 4 Chamber Apical View

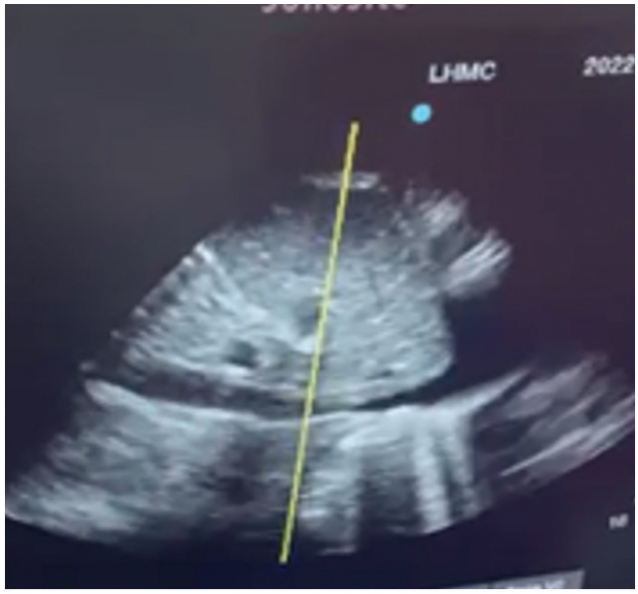


Fig 7: Subcostal IVC view

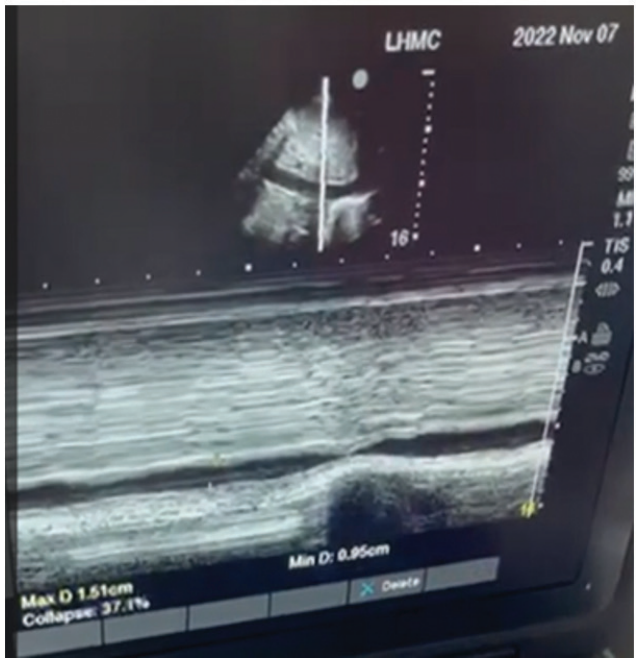


Fig 8: M Mode IVC CI measurement

The long parasternal view(PLAX) gives a view of the left atria, left ventricle, mitral valve, right ventricle, aortic root, aortic valve, aortic outflow tract. This view is useful for estimation of left ventricular ejection fraction(LVEF) by observing the intensity of cardiac contractility during the cardiac cycle. With experince a normal contracting heart can be differentiated from a hypokinetic heart as seen in acute decompensated heart failure (ADHF). Another method of of assessing the LVEF is by observing the excursion of the anterior mitral leaflet during diastole. If it only moves less than half way towards the AV septum than LVEF is reduced. Reduced LVEF is seen in PPCM and acute HF secondary to cardiac lesions.

The right ventricular chamber is normally ⅔ the size of the left ventricular (LV) chamber. An increase in this ratio, or bowing of the interventricular septum towards the left side of the heart indicates that right heart outflow is obstructed causing increased RV pressure resulting in enlargement of the RV. In the short parasternal view the crosssectional view of right and left ventricle is obtained. The same findings of increased RV pressure pushing the interventricular septum towards the LV gives rise to the D sign. These features are observed in pulmonary embolism or amniotic fluid embolism .

When a right ventricular dilatation or right heart strain pattern is observed on FoCUS a simultaneous compression USG of the femoral /popliteal vessels should be performed for presence of deep vein thrombosis.

Intravascular Volume Status

IVC Collapsibility Index(CI) and IVC diameter are used to determine volume status . Diameter of IVC is measured just below the entry of hepatic vein into the IVC which corresponds to approximately 2 cm from the atrium. M Mode is used to measure the maximum and minimum diameter of IVC through the respiratory cycle which give the collapsibility index. An IVC diameter of >2.1 cm and CI of <50% is suggestive of elevated right atrial pressure (RAP) of 15mmHg (10-20mmHg) and IVC diameter of <2.1cm and CI>50% suggests normal pressure. Elevated RAP demands fluid restriction. In preeclampsia presence of B Lines and increased RAP are indicators of impending pulmonary edema

Important Causes of Acute Dyspnea in Obstetric Patients

1. Pulmonary Embolism

In 65% of patients, PE is suspected because of pleuritic chest pain which may be accompanied or not by dyspnea. Symptomatic PE may present as three distinct syndromes of different pathology and variable severity.

This typically presents with pleuritic pain due to irritation of the visceral pleura and rarely hemoptysis. The classical radiological picture is a wedge-shaped pleural-based infiltrate that affects approximately 20% of patients.

Isolated dyspnea: The absence of systematic pleuritic pain in this syndrome is likely due to a more proximal embolization level in the pulmonary vasculature.

Patients may complain of oppressive retrosternal chest pain.

Syncope and/or shock are the clinical manifestations of massive pulmonary embolism causing acute severe pulmonary hypertension and right ventricular failure. It is usually due to large central clots. The investigations and management for suspected pulmonary embolism are shown in Figure 9.

Clinical features: Pregnant/postpartum women with sudden onset dyspnoea, tachypnoea, chest pain, tachycardia with or without hemodynamic compromise: Suspect Pulmonary embolism

Investigations

1. ECG
2. Bedside C-Xray
3. Bedside lung ultrasound : to rule out other pulmonary pathology
4. Focused cardiac USG – Dilated Right ventricle-D Sign
5. D-Dimer 100 negative predictive value
6. CTPA , VQ Scan : confirmatory
7. Compression USG
8. CTPA

Management :

Stable patient : Unfractionated Heparin 80U/kg bolus followed by 18U/Kg/ hour or LMWH 1mg/kg every 12 hours.

Massive PE : Acute severe pulmonary HTN/Right ventricular failure/hemodynamic instability : Thrombolysis with alteplase

Figure 9: Investigations and Managemnt of Pulmonary Embolism

2. Pulmonary Edema

Diagnosis is on basis of history, examination, and lung ultrasound and/or Chest X-Ray.

History of breathlessness, orthopnea, tachypnea, pinky frothy secretions with clinical findings of use of accessory muscles of respiration, bilateral basal crepitations and reduced SpO_2 at initial assessment will further propel towards considering pulmaonary edema as a diagnosis.

Pulmonary edema in pregnancy could be cardiogenic or non cardiogenic

Preeclampsia is the commonest predisposing factor which may have both cardiogenic and non cardigenic factors contributing to pulmonary edema (Table 4).

Peripartum cardiomyopathy (PPCM) is also another important and common cause of cardiogenic pulmonary edema (Box 1)

Box 1: Diagnosis of PPCM

Peripartum Cardiomyopathy (PPCM) is diagnosed when heart failure secondary to left ventricular systolic dysfunction with LVEF < 45% occurs in the last month of pregnancy or in the months following delivery with no other identifiable cause of HF .

Investigations for diagnosis of cardiac cause of pulmonary oedema include bedside ECG, CXR, ProBNP/BNP and Cardiac POCUS initially followed by detailed ECHO later.

Table 4: Causes of Pulmonary Edema in Pregnancy

Cardiogenic pulmonary edema	Non cardiogenic pulmonary edema
• Rheumatic heart disease: MS, MR, AS,AR • Cardiomyopathy: Dilated, hypertrophic, peripartum • Congenital heart disease • Ischemic heart disease • Arrythmias • Hypertensive heart disease • Preeclampsia, eclampsia • Severe Anaemia • Thyrotoxicosis	• Preeclampsia, eclampsia • Fluid overload • Drugs like tocolytics, oxytocin • Sepsis • Transfusion relates acute lung injury (TRALI) • ARDS • Pneumonia

The management of pulmonary edema is discussed in Box 2

Box 2: Managent of Pulmonary Edema

- Inj. Frusemide
- Inj. Nitroglycerin infusion is a preferred antihypertensive for control of BP in women with pulmonary oedema. Nitrates also are drug of choice for non hypertensive heart failure as it decrease preload and afterload and reduces workload on heart.
- Inj. Hydralazine reduces afterload. It may be added along with nitrates as it reduces the development of tolerance to nitrates .
- In postpartum patients : ACE, Angiotensin receptor blockers (ARBs), Angiotensin receptor-neprilysin inhibitors (ARNIs), B Blockers : Carvedilol, Metoprolol may be used.
- Maintain Oxygenation –NIV/Invasive ventilation
- For unstable patients with cardiogenic shock : Inotropes/ vasopressors
- If not already delivered consider delivery in refractory pulmonary oedema. Expedite delivery after maternal stabilization

In PPCM the treatment is summarized by the acronym "BOARD": Bromocriptine, Oral Heart failure drugs, Anticoagulants, Relaxants (intravenous vasodilators), Diuretics.

3. Amniotic Fluid Embolism

It is a life threatening disorder causing cardiorespiratory

failure during labour or within 30 minutes of delivery. The presentation is acute though patients may not manifest all features given below, some rapidly deteriorate and sustain cardiac arrest. The typical clinical features are described in Box 3.

Box 3: Clinical Features of Amniotic Fluid Embolism

- Acute hypoxia (with dyspnoea, cyanosis and/or respiratory arrest),
- Rapid onset of acute hypotension and/or cardiac arrest
- Coagulopathies (or severe haemorrhage),
- Coma and seizures.

Pathophysiology: Breach of barrier between maternal blood and amniotic fluid and resultant entry of amniotic fluid debris into the systemic circulation causes physical obstruction of the pulmonary circulation.

The second hypothesis - entry of amniotic fluid into the maternal circulation activates inflammatory mediators, causing a humoral or immunologic response called as the "anaphylactoid syndrome of pregnancy"

Management of AFE is discussed in Box 4 as shown below.

Box 4: Management of Amniotic Fluid Embolism

- Correction of hypoxia may require mechanical ventilation
- Vasopressor noradrenaline 0.05-3.3 µg/kg/min,
- Inotropes : Dobutamine 2.5-5 µg/kg/min, Milrinone 0.25-0.75 µg/kg/min,
- Pulmonary vasodilators : Inhaled Nitric Oxide/Inhaled Epoprostanol, IV Epoprostanol/Sildenafil ,
- Massive transfusion protocol for bleeding and coagulopathy. : PCV, FFP/Cryoprecipitate, Platelets, fibrinogen and tranexamic acid.
- Thromboelastography can help guide replacement
- ECMO in refractory right heart failure

4. Adult Respiratory Distress Syndrome

In 2012, the clinical criteria for diagnosis of ARDS was defined by Berlin definition as shown in Box 5. The treatment is discussed in Box 6.

Box 5: Berlin Citeria for ARDS

It manifests as non cardiogenic pulmonary oedema . The most common etiological factor is sepsis in 50% of cases. Other causes are aspiration pneumonitis, pneumonia, pancreatitis and trauma and other causes of noncardiogenic pulmonary oedema like amniotic fluid embolism, TRALI, preeclampsia, acute fatty liver of pregnancy

Box 6: Treatment of ARDS

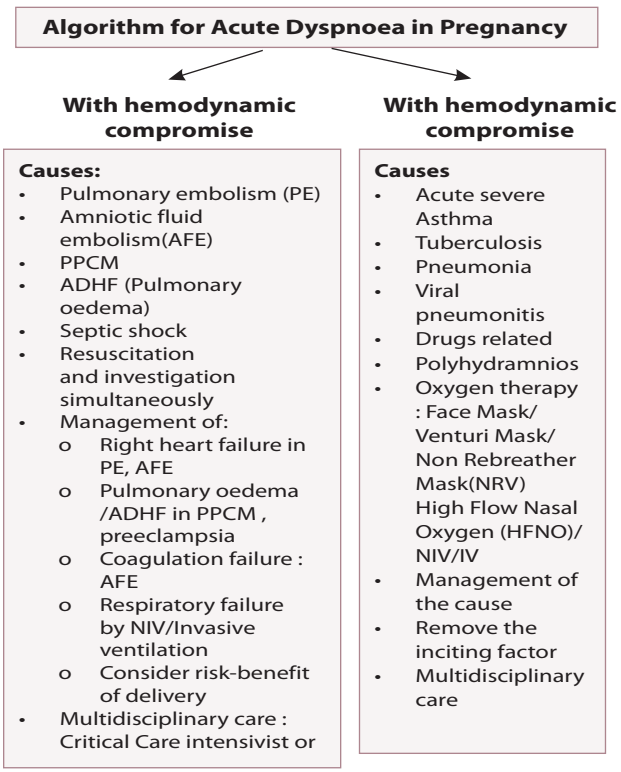
Treatment :

- Non-invasive ventilation /High-Flow oxygen therapy for mild cases
- Lung protective mechanical ventilation with lower tidal volumes and higher levels of positive end-expiratory pressure in moderate-to severe ARDS.
- Prone position ventilation redistributes alveolar stress, realigns transpulmonary pressure in the ventral-dorsal direction leading to increase alveolar recruitment.
- Pharmacotherapy : Diuretics, Corticosteroid, Inhaled Nitric oxide/epoprostenol2
- Veno- Venous Extracorporeal membrane oxygenation may be required for resistant cases.
- Consider delivering the foetus if invasive ventilation is required and baby is viable
- Eliminate the inciting factor

Other important causes of acute dyspnoea in pregnancy is acute severe asthma managed by inhaled steroid and B2 agonists, ipratropium bromide, systemic corticosteroids, oxygen therapy

Undiagnosed tuberculosis can present with acute dyspnoea and respiratory failure in pregnancy. Long cough and evening rise of temperature, loss of weight and appetite and a history of contact with infected person may give a clue. CxR and sputum for AFB or bronchial washings for CBNAAT are investigations of choice.

In women with fever, cough and breathlessness viral and bacterial pneumonia should be also considered.



Key Points

- Acute Dyspnoea in pregnancy may be due to pulmonary, cardiac, obstetric or miscellaneous causes
- Early diagnosis through point of care tests like bedside ABG, ECG , CxR and POCUS and early initiation of appropriate management will minimize adverse outcome. Skills in performing bedside tests like POCUS and knowledge of interpretation of beside test (ABG, ECG, CXR) should be included in residency program as a part of critical care obstetrics
- Termination of pregnancy should be considered if pregnancy compromises the cardio-pulmonary system

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Pregnancy Related Acute Kidney Injury- Prevention is Better Than Cure

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What is PRAKI?

PRAKI refers to Pregnancy Related Acute Kidney Injury, which is acute kidney injury (AKI) occurring during pregnancy or within 6 weeks post-partum. Renal disorders in pregnancy include asymptomatic bacteriuria, acute kidney injury (PRAKI), chronic kidney disease, renal disease requiring dialysis, acute cortical and tubular necrosis, end stage renal disease, pregnancy after renal transplant, glomerulonephritis and nephropathy due to collagen vascular diseases.

Around 10% of the intensive care unit (ICU) admissions in developing countries are obstetric patients. AKI accounts for 5% of hospital admissions but 30% of ICU admissions in India. Although the incidence of PRAKI is rare, it can cause potentially adverse maternal and fetal/neonatal outcomes. Managing a critically ill obstetric patient poses a challenge for the obstetrician and requires a good understanding of pregnancy-related physiological changes and pregnancy- specific illnesses. Table 1 summarises the normal physiological changes in the renal system during pregnancy.

Table 1: Renal Physiology during Pregnancy

	Renal	Renal Hemodynamics	Cardiovascular	Volume hemostasis	Acid-Base Balance
↑	-Size and volume of kidney, collecting system -Glomerular membrane porosity -Ureteral smooth muscle hypertrophy	-RPF (50-85%) -GFR (40–65%) - Creatinine clearance - Filtration of sugar, protein	-Stroke volume -Cardiac output	-Total body water (6.5L at term) -Plasma volume (40-50%)	- pH (7.42-7.46) - Bicarbonate reabsorption
↓		-Renal vascular resistance	-systemic vascular resistance	-plasma osmolality (by 10 mOsm/kg) - s. albumen	-pCO2 (18–22 mmol/L)

RPF- renal plasma flow, GFR- glomerular filtration rate

Incidence of PRAKI

The incidence of PRAKI in developed countries in 1 in 20,000 pregnancies, which has further decreased 10 folds over the years. In developing countries, however, it still contributes to significant maternal and neonatal health burden. The incidence of PRAKI in India has declined from 22% in 1960 to 3–7% in 2000s. This has occurred as a result of better quality of antenatal and post-partum care, and decreasing incidence of septic abortion. Hence, it is important to be aware of the causes of AKI in pregnancy and the measures that can be taken to prevent it.

Till date, there has been no consensus on a standard definition of PRAKI. Following table [Table 2] depicts the commonly used classification systems for defining AKI in non-pregnant adults. The same definitions have been adopted to define pregnancy related AKI as well.

Table 2: AKI definition, classification and staging systems

AKI definition, classification and staging systems								
RIFLE criteria			**AKIN criteria**			**KDIGO criteria**		
Stage	**Increase In s. Cr.**	**Urine output**	**Stage**	**Increase In s. Cr.**	**Urine output**	**Stage**	**Increase In s. Cr.**	**Urine output**
R	X1.5	<0.5 ml/kg/h for 6-12h	1	≥ 1.5–2.0 × or ≥ 0.3 mg/dL	< 0.5 ml/kg/h for 6-12h	1	≥ 1.5–1.9 × or ≥ 0.3 mg/dL	< 0.5 ml/kg/h for 6-12 h
I	X2.0	< 0.5 ml/kg/h for 12 h	2	≥ 2.0-3.0	< 0.5 ml/kg/h for 12 h	2	≥ 2.0–2.9 × or ≥ 3 mg/dL	< 0.5 ml/kg/h for 12 h
F	X3.0 Or s. Cr >4mg/dl	< 0.3 ml/kg/h for 24 h or anuria for 12 h	3	≥ 3.0 × or ≥ 4 mg/dL or received RRT	< 0.3 ml/kg/h for 24 h or anuria for 12 h	3	≥ 3.0 × or ≥ 4 mg/dL or received RRT	< 0.3 ml/kg/h for 24 h or anuria for 12 h
L	Persistent ARF>4 weeks							
ESKD	ESKD > 4 months							

RIFLE- risk (R),injury (I),failure (F),loss (L),ESKD; AKIN- acute kidney injury network, KDIGO- Kidney Disease Improving Global Outcomes, ESKD- end stage kidney disease, s. Cr.- serum creatinine, GFR- glomerular filtration rate; x – times; RRT- renal replacement therapy

Causes of PRAKI

The etiology of PRAKI is multifactorial, the risk factors and causes of PRAKI being diverse. They can be grouped into: Prerenal, renal and post-renal causes [Table 3].

Table 3: Causes of PRAKI

Causes of PRAKI
PRERENAL CAUSES*
Pregnancy-related conditions
Hypovolemia due to water loss
Hyperemesis gravidarum
Vomiting due to preeclampsia, HELLP, and AFLP
Hypovolemia due to hemorrhage
Early pregnancy bleeding (abortion, ectopic, molar pregnancy) APH, Placental abruption APH, Placenta previa PPH (Uterine atony, Bleeding during surgery, Uterine laceration) Uterine rupture/perforation
Hypotension due to decreased effective circulating volume
Septic abortion
Puerperal sepsis
Pregnancy-unrelated conditions
Acute gastroenteritis (AGE)
Pyelonephritis/Urosepsis
RENAL CAUSES
Pregnancy-related conditions
Preeclampsia, Eclampsia and HELLP Syndrome AFLP
Hepatorenal syndrome (HRS)
Hemolytic uremic syndrome (HUS)? Thrombotic thrombocytopenic purpura (TTP)
DIC
Glomerulonephritis
Autoimmune disorders
POST-RENAL CAUSES
Pregnancy-related conditions
Multifetal gestation
Trauma to the ureters and bladder during caesarean section
Pregnancy-unrelated conditions
Renal/ ureteral stones
Large uterine fibroid

Prerenal causes like haemorrhage and sepsis account for nearly half the cases of PRAKI in developing countries. This is in stark contrast to developed countries, where the leading causes for PRAKI are renal such as like pre-eclampsia, eclampsia, chronic hypertension, and renal disease. Conditions like Haemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, acute fatty liver of pregnancy (AFLP), and thrombotic microangiopathy (TMA) may also sometimes lead to PRAKI in the peripartum period.

A study conducted in a tertiary care hospital in Delhi catering to critically ill patients of PRAKI of North India reported that 84% of the patients had pre-renal causes for pregnancy related AKI. As many as a quarter of the patients presented to the hospital in shock, 37% patients needing dialysis and a third of the patients succumbing to the complications of AKI. The leading causes of PRAKI in this study were antepartum haemorrhage and post-partum haemorrhage.

Pathophysiology of Pre-Renal PRAKI

Hypovolemia and haemorrhage leads to renal hypoperfusion resulting in prerenal azotemia. Acute loss of blood volume leads to decreased glomerular filtration rate which in turn activates renin-aldosterone-angiotensin-system and renal baroreceptors. This further results in acute 'renal shutdown' in order to increase peripheral resistance. It also causes fluid retention, thus maintaining perfusion to vital organs. Hypovolemia, thus, leads to renal hypoxia causing kidney injury. On the other hand, renal causes of AKI cause direct injury to glomerulus or renal tubules. Commonly seen renal causes of PRAKI in Indian population are hypertensive disorders of pregnancy particularly pre-eclampsia, eclampsia, HELLP syndrome and associated placental abruption which acts as both prerenal and renal cause of AKI. Sepsis is also an important cause of AKI in the peripartum period and leads to direct renal injury.

Management of PRAKI

The bundles of care of PRAKI revolve around supportive treatment. It requires hemodynamic stabilisation which is of critical importance as autoregulatory mechanisms are impaired in AKI. Nephrotoxic drugs should be discontinued and dose of medications affecting renal function should be adjusted. Antibiotic initiation is a critical step in case of septicemia. Rapid identification and treatment of AKI complications such as hyperkalemia, metabolic acidosis, anemia, and fluid overload is important. Fluid balance should be optimised and carefully titrated as per individual. Fluid therapy is directed by the fluid responsiveness of the individual. Table 4 outlines the principles of management of AKI.

Table 4: Management of PRAKI

Management of PRAKI	
General Principles	**Specefic management**
Stabilize the patient	Patient vitals, intake-output
HDU/ICU care	Assessment of respiratory, circulatory, and haemodynamic systems
Involve nephrologists	CBC, Blood group, KFT with SE, ABG (where necessary), USG-KUB
Treat the pathology	Volume resuscitation- oral fluids (where possible), i/v crystalloids and colloid, blood products
Avoid nephrotoxic drugs	Treat underlying cause- antihypertensive, delivery
Prevent further kidney damage	Loop diuretics
Supportive care for mother (priority)	Low dose dopamine infusion
Monitor fetal well-being	Renal Replacement Therapy (where necessary)
	Correction of acid-base imbalance
	Correct dyselectrolytemia

Can PRAKI be prevented?

Just like most developing countries, in the Indian setup, majority cases of PRAKI are due to prerenal causes like obstetric haemorrhage and hypovolemia which is largely preventable. The two prongs to preventing pre-renal AKI are early and timely recognition of hypovolemia and its prompt correction. As elaborated in Table 2, there are various classification systems which not only define criteria for the diagnosis of AKI, but also have stages which correlate with severity of kidney injury, reversibility and associated morbidity or mortality of the patient. The Kidney Disease Improving Global Outcomes (KDIGO) Initiative Group combines two previously used classification systems, namely RIFLE and AKIN criteria. It divides AKI into 3 stages based on urine output and serum creatinine levels. Stage I is reversible and associated with lower risk of mortality, whereas, as the stage progresses, specially stage III, it tends to be irreversible and associated with higher mortality, emphasizing on the need for early intervention in cases of hypovolemia. Simple measures like strict intake output monitoring and measures to aggressively resuscitate the patient with IV fluids and/or blood products can prevent acute kidney injury from developing, reverse early stages of AKI and prevent further complications of AKI. Prevention

of AKI requires recognition of at-risk patients and directing the therapy at correcting the modifiable risk factors. The gold standard preventive strategy for pre-renal AKI is hemodynamic and volume status optimisation. Avoiding the use of nephrotoxic drugs in such individuals should be considered. Here's a list of common obstetric conditions that can be complicated by AKI and how AKI can be prevented in these [Table 5].

Table 5: Preventing AKI in Commonly Observed Obstetric Conditions

Condition	Mechanism of AKI	Preventive Strategies for AKI
I trimester		
Hyperemesis Gravidarum	Pre-renal (dehydration, hypovolemia) Renal (acute tubular necrosis)	Monitoring vitals, Intake-output, KFT & SE Hydration (oral if tolerated/IV fluids) Correction of electrolyte imbalance Anti-emetic therapy Correction of any underlying cause of vomiting
Septic abortion	Pre-renal azotemia, hypovolemia) or Renal (acute tubular necrosis, intra-renal inflammation)	Fluid replacement Monitoring vitals, Intake-output Antibiotics and source control of infection (surgical intervention where needed) Vasopressors (where needed, to maintain arterial pressure)
II/III trimester/ Peripartum		
Urinary tract infections/ pyelonephritis	Renal	Urine routine and culture- screen every trimester to treat asymptomatic bacteriuria Early aggressive antibiotic therapy Adequate fluid replacement Repeat Urine culture after treatment
Preeclampsia/ HELLP	Renal Thrombotic microangiopathy (HELLP)	Predicting preeclampsia early (uterine artery PI, PAPP-A, PIGF. sFlt-1/PlGF ratio) Starting low dose aspirin (preventing preeclampsia/reducing its severity thus reducing its complications) Baseline KFT, Monitor urine output Anti-hypertensives Urine output monitoring and baseline KFT in patients on magnesium sulphate USG-KUB in chronic hypertensives Delivery (as indicated as per period of gestation and severity)
Sepsis	Prerenal azotemia Renal (acute tubular necrosis)	Fluid replacement Monitoring vitals, Intake-output Antibiotics and source control of infection (surgical intervention where needed) Vasopressors (where needed, to maintain arterial pressure)
Acute gastroenteritis (any trimester)	Pre-renal (dehydration, hypovolemia)	Monitoring vitals, Intake-output, KFT & SE Hydration (oral if tolerated/IV fluids) Correction of electrolyte imbalance Anti-emetic therapy Correction of cause of gastro-enteritis, Antibiotics
Antiphospholipid Antibody Syndrome (APLA)	Renal (acute tubular necrosis, microangiopathy)	Aspirin Low molecular weight heparin
Acute fatty liver of pregnancy (AFLP)	Renal (deposit of free fatty acids in renal tubules)	Urgent delivery Supportive care
Hydronephrosis Renal calculi	Post renal (uereteric compression by gravid uterus, urinary stasis, urinary tract infection)	Ureteral stent placement and reliving the compression

Peripartum haemorrhage- antepartum haemorrhage	Prerenal (hypovolemia)	Assessing blood loss (specially concealed abruption), vitals, shock index Correction of anemia (antenatally) Fluid therapy and blood replacement Monitor vitals, intake output Ultrasound antenatally- placental localisation, diagnosing placenta accrete spectrum Delivery in a tertiary care centre (high risk- placenta previa, placenta accrete)
Peripartum haemorrhage- post-partum haemorrhage (PPH)	Prerenal (hypovolemia)	Correction of anemia (antenatally) Active management of third stage of labour- prevent PPH At risk patients- readiness Interventional radiological techniques like catheter placement for uterine artery embolisation Recognising PPH and assessing blood loss, vitals, shock index Fluid therapy and blood replacement Monitor vitals, intake output Control bleeding- Medical management Other measures- tamponade, surgical measures

Conclusion

The incidence of PRAKI is higher in developing countries compared to developed countries. It significantly impacts the maternal and fetal outcomes. Most cases of PRAKI in developing countries such as India are due to pre-renal causes like obstetric haemorrhage and hypovolemia due to dehydration which are largely preventable. Renal causes like preeclampsia and sepsis are important intra-renal causes of AKI. Early recognition of these conditions, prompt correction of hypovolemia by fluids, oral rehydration or blood transfusion and timely referral to a higher centre for appropriate management are crucial in reducing the incidence of AKI as well as in preventing its complications.

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Diabetic Ketoacidosis in Pregnancy: Recognition and Response

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Introduction

Pregnancy complicated by diabetic ketoacidosis (DKA) is a rare but critical condition that can be life-threatening. Although more commonly observed in women with type 1 diabetes, DKA can also develop in those with type 2 or gestational diabetes. DKA affects 0.5-8.9% of all Diabetic Gestations. Management of DKA in this population poses unique challenges, as it can arise at lower blood glucose levels than in non-pregnant individuals and necessitates careful attention to both maternal and fetal health due to the potential for complications in both. The condition also carries substantial risks for maternal morbidity and stillbirth. Fetal mortality is 9-36% and maternal mortality is <1%.

Pathophysiology of DKA in Pregnancy (DKP)

Pregnancy is a ketogenic state, women with type 1 diabetes, and to a lesser extent, those with type 2 or gestational diabetes, are at risk for diabetic ketoacidosis (DKA) at lower blood glucose levels than non-pregnant individuals.

Several physiological changes during pregnancy contribute to this increased risk, including:

- reduced buffering capacity from respiratory alkalosis in pregnancy and subsequent decreased bicarbonate levels,
- relative insulin resistance combined with increased lipolysis and free fatty acids, and
- further reduced insulin sensitivity from elevated human placental lactogen, progesterone, and cortisol levels. (Figure 1)

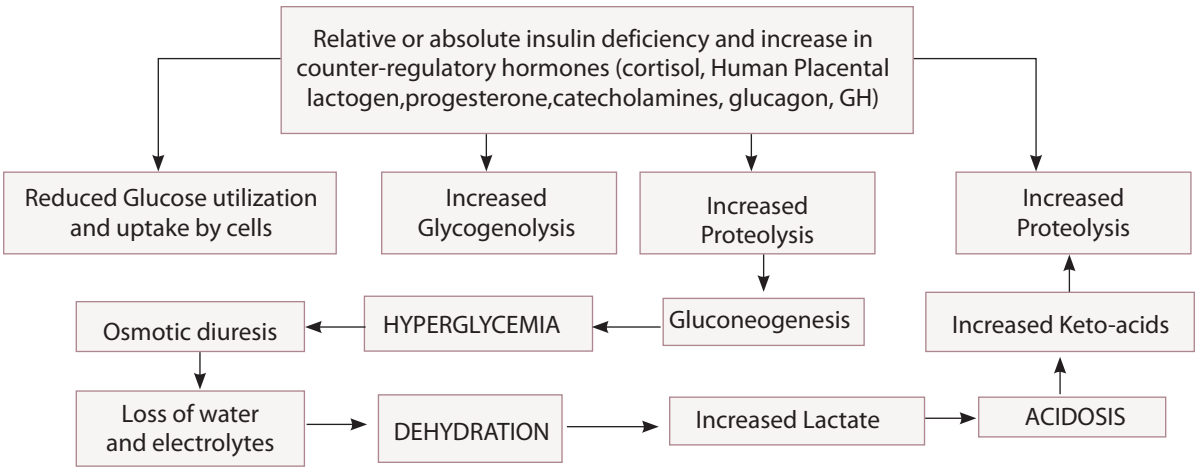


Fig 1: Pathophysiology of DKP

Precipitating Factors of DKP: Factors that lead to absolute or relative insulin deficiency:

- Protracted vomiting /hyperemesis gravidarum (55%)
- Non-compliance with insulin (45%)
- Poor glycemic control (25%)
- Insulin non-compliance/ pump failure
- Infections and sepsis
- Medications precipitating DKA such as beta agonists, steroids
- Conditions such as diabetic gastroparesis

Clinical Diagnosis

Pregnant women presenting with the following **signs and symptoms** should be suspected with DKA:

- Nausea, vomiting and abdominal pain (may mimic acute abdomen)
- Signs of dehydration
- Tachypnea, Deep sighing breathing (Kussmaul's respiration)
- Polyuria, polydipsia
- Drowsiness, lethargy, blurred vision Confusion, altered sensorium, change in mental state

- Muscle weakness
- Hypotension, tachycardia
- Shock
- Coma
- Abnormal CTG

When DKP is suspected, the following **investigations** are required to confirm the diagnosis, assess the severity and cause/ precipitating factors.

1. Serum/urine ketones
2. Blood Glucose [more than 200 mg/dl (DKP can even occur at lower glucose levels)]
3. Blood Gas Analysis to look for
   - Serum bicarbonate (less than 15 mEq/l)
   - pH (less than or equal to 7.30)
   - Anion gap more than 20 (HAGMA)
   - Elevated base deficit ≥4 mEq/l
   - Lactate levels
4. Serum Electrolytes to look for hypokalemia (Potassium level may be falsely normal/elevated)

Diagnostic Criteria:

Diagnosis is based on the triad of **hyperglycemia, ketosis and metabolic acidosis**. The Joint British Diabetes Societies Inpatient Care Group guidelines state the following diagnostic criteria for DKP:

1. Blood ketone ≥ 3.0 mmol/l (or) urine ketones > 2+
2. Blood glucose >200 mg/dl (11.0 mmol/l) or known diabetes mellitus
3. Bicarbonate > 15.0 mEq and/or venous pH less than 7.3

The degree of acidosis can be used to categorize the **severity of DKA**.

- Mild: pH < 7.3
- Moderate DKA: pH < 7.2
- Severe DKA: pH < 7.1

Management of DKP

Diabetic ketoacidosis (DKA) in pregnancy is an emergency requiring immediate recognition and resuscitation by a multidisciplinary team in a high dependency or intensive care unit.

Critical initial steps involve securing large-bore intravenous access or a central line, along with continuous maternal monitoring via cardiac monitoring and pulse oximetry. Management encompasses six main aspects that should be addressed simultaneously.

Fluid resuscitation must always precede the initiation of insulin therapy.

The six arms of management of DKA

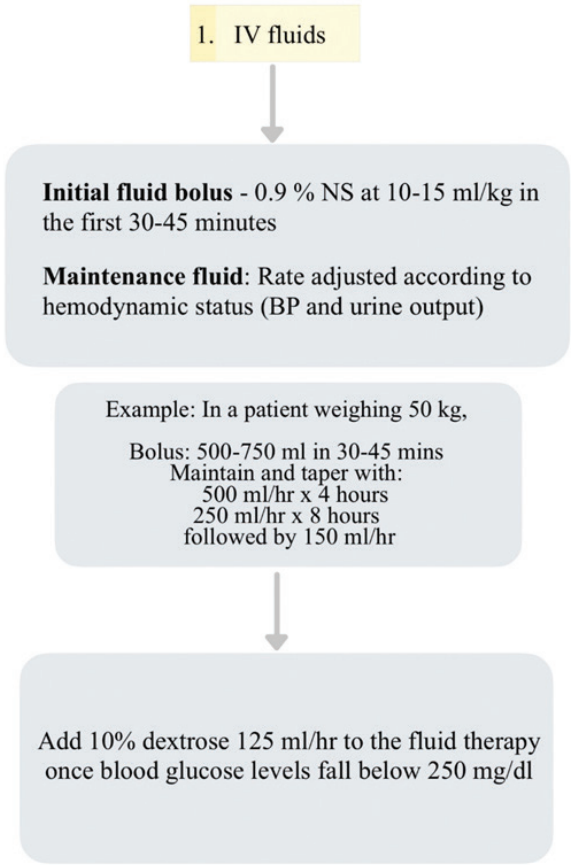
1. **Intravenous fluid replacement:** This is essential in DKA management to improve perfusion, decrease stress hormones, cause hemodilution, and lower hyperglycemia, thus improving insulin's effectiveness.

   Rehydration must occur before insulin therapy, aiming to replace the approximate 100 ml/kg fluid deficit within 24-48 hours.

   Fluid of choice for resuscitation: 0.9% Normal Saline.

   Initial treatment involves 10-15 ml/kg boluses over 30-60 minutes, followed by maintenance fluids guided by hemodynamic status, using blood pressure, urine output and sometimes CVP to assess response. For SBP <90 mm Hg, administer 1L normal saline over 30 minutes, repeating if needed. Once SBP >90 mm Hg, maintain with normal saline: 1 L/ hour for 1 hour, then 500 ml/hour for 4 hours, 250 ml/hour for 8 hours, and then 150 ml/hour.

   Add 10% dextrose at 125 ml/hour when glucose <250 mg/dl. Caution is needed in patients with heart or kidney disease to prevent fluid overload.



2. **Electrolyte correction**: Insulin induces the intracellular movement of potassium; hence it is crucial to correct any pre-existing hypokalemia before initiating insulin therapy. Insulin administration can worsen hypokalemia and may lead to life-threatening cardiac arrhythmias.

While awaiting serum electrolyte results, potassium levels from arterial blood gas (ABG) can provide initial guidance for therapy.

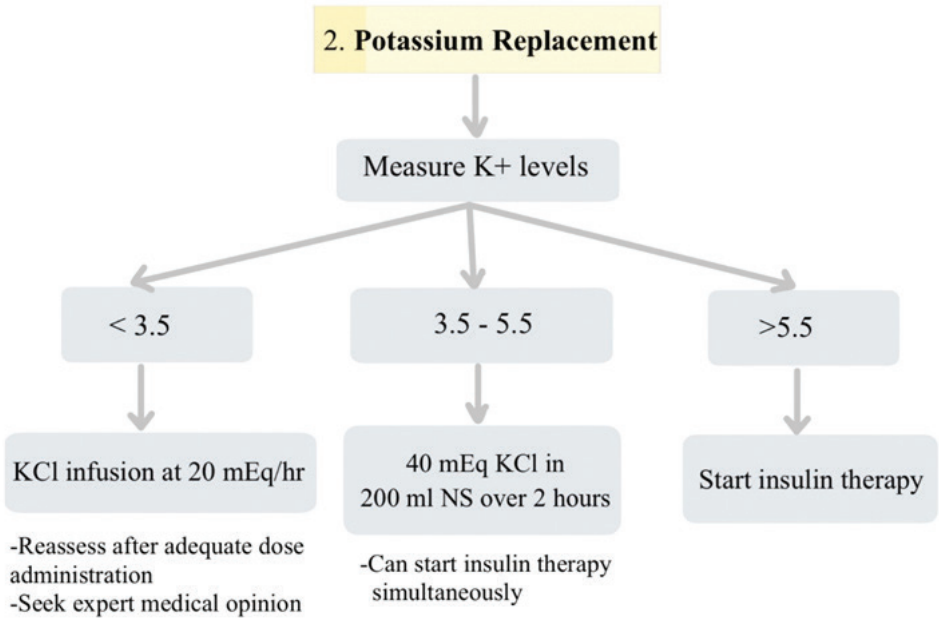
Intravenous KCl administration necessitates adequate urine output (>0.5 ml/kg/hr.)

The management of potassium levels is as follows:

- K+ is greater than 5.5 mEq/l: KCl is not needed, and insulin can be started;
- K+ is between 3.5 and 5.5 mEq/l: administer 40 mEq of potassium chloride in 200 ml of IV normal saline over 2 hours, at a rate under 20 mEq/hr through a peripheral line;
- K+ is less than 3.5 mEq/l: infuse KCl at 20 mEq/hr via a peripheral line.

For patients needing higher KCl infusion rates or doses (upto 60 mEq/hr), a central line should be used. Expert consultation is advised for patients requiring these higher doses.

Each KCl ampoule (20 mEq) will raise serum potassium by 0.25 mEq/l. The maximum potassium dose in 24 hours should not exceed 160 mEq. Further correction can be guided by serial 6-hourly venous blood gas (VBG) measurements.



3. **Intravenous insulin:** Insulin is required in DKA to address reduced circulating insulin and increased counter-regulatory hormones. Although rehydration lowers blood glucose, insulin therapy is essential for restoring cellular metabolism, suppressing lipolysis and ketogenesis, and normalizing glucose levels. Important points for correction of insulin deficiency are:

- Insulin infusion is usually started 1 hour after initiation of IV fluid treatment and after correction of hypokalemia, if any
- Dose: Regular insulin infusion is started at a fixed rate of 0.1 unit/kg/h. Initial rate should not exceed 15 units/h.
- If the patient is already maintained on basal insulin e.g. detemir or glargine, then this should be administered concomitantly with the IV insulin infusion. This leads to a smooth transition to subcutaneous insulin after resolution.
- Route of administration: Intravenous (IV)
- An IV insulin bolus should not be used at the start of therapy as it can precipitate shock by rapidly decreasing osmotic pressure and can exacerbate hypokalemia.
- To ensure accurate insulin delivery during intravenous infusion, priming the tubing with the insulin solution is essential.
- When peripheral intravenous access is compromised by severe dehydration, intramuscular administration can be considered.

- The use of central venous lines for insulin delivery is discouraged due to the inherent dead space within these lines, which can result in unpredictable insulin dosing.

The **metabolic targets** with initial intravenous insulin therapy:

- Decrease in blood ketone levels by 0.5 mmol/l/h
- Increase in venous bicarbonate levels by 3 mEq/l/h
- Decrease in capillary blood glucose levels by 54 mg/dl/h

If the metabolic targets (biochemical improvement) cannot be achieved by the current infusion rate, the insulin infusion rate should be increased by 1 unit/h until ketones reach the desired level.

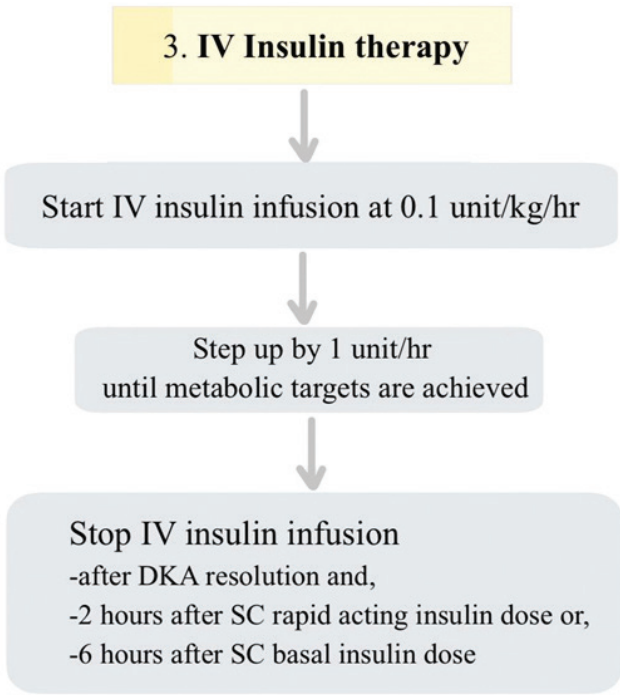
The DKP resolution criteria consist of:

- Blood ketone level less than 0.6 mmol/l
- pH more than 7.3
- Serum bicarbonate more than 15 mEq/l
- Normalisation of the anion gap (less than or equal to 12 mEq/l)
- Clinical improvement in patient general condition, mentation.

The introduction of oral fluids should be reserved until substantial clinical improvement is evident (mild acidosis or ketosis may still be present). It is important to note that the measurement of urine ketones using rapid test strips detects only acetoacetate and acetone. Thus, persistent ketonuria may be observed for several hours following the normalization of serum 3-beta-hydroxybutyrate (3-BOHB) levels. The absence of ketonuria should not be used as the sole determinant for DKA resolution.

Once DKA resolution criteria are met, i.e. ketoacidosis has resolved and oral intake is tolerated, the change to SC insulin is planned. Conversion from intravenous to subcutaneous insulin dosing may be guided by the following:

- Start subcutaneous insulin 2 h prior to discontinuing intravenous insulin infusion (overlapping)
- Ensure insulin regimen provides 24 h coverage
- Basal and rapid-acting insulin analogues are preferred (once or twice daily basal insulin + mealtime rapid-acting insulin)
- Total daily insulin dose (TDD) of regular insulin over the last 24 hours is divided into 1:1 ratio – with 40–60% of TDD given as basal insulin + remaining proportion divided into three pre-meal time doses of rapid-acting insulin.
- Overlapping is done to prevent rebound hyperglycemia. The first SC injection should be given 1-2 hours (with rapid-acting insulin) or 6-12 hours (with long acting insulin) before stopping the insulin infusion to allow sufficient time for the subcutaneous insulin to be act. The rate of IV insulin administration is gradually decreased.
- After transitioning to SC insulin, frequent blood glucose monitoring is required to avoid marked hyperglycemia and hypoglycemia.



4. **Evaluation for bicarbonate therapy:** The use of bicarbonate in DKA management is generally discouraged due to potential harm to both the patient and the fetus.

- Bicarbonate administration can inhibit compensatory hyperventilation, which is essential for carbon dioxide elimination, potentially leading to increased PCO2 and decreased fetal oxygen delivery.
- Furthermore, it may contribute to paradoxical cerebral acidosis, as CO2 diffuses across the blood-brain barrier more rapidly than infused bicarbonate, and
- it can also delay ketone clearance and worsen hypokalemia.

However, bicarbonate administration may be necessary in cases of severe DKA (pH <7.1).

Typically, the acidosis associated with DKA is corrected through fluid and insulin therapy,

with ketone clearance. The most common cause of unresolved acidosis is the development of hyperchloremic acidosis (normal anion gap metabolic acidosis) secondary to the administration of large volumes of normal saline, which has a high chloride content. This condition is usually benign and should not delay the transition to subcutaneous insulin. Insulin therapy does not play a role in correcting hyperchloremic acidosis. Infrequent causes of persistent acidosis include inadequate fluid administration, infection/sepsis, and errors in the preparation of intravenous insulin infusions.

5. **Identification and management of precipitating factors:** Recognizing the underlying condition that triggers DKP is crucial for its effective management, as any delay in addressing the precipitating factor can lead to a worsened prognosis and increased risk of recurrence. All known precipitating factors must be ruled out by comprehensive patient history taking and physical examination followed by guided investigations aimed at targeting the underlying cause. A detailed clinical evaluation to rule out infection should be conducted, and appropriate management and antibiotics should be initiated if an infection is suspected.

6. **Monitoring of mother and fetus and planning the delivery:**

- Hourly capillary blood glucose should be monitored during insulin infusion.
- Blood ketones should be monitored hourly for the first 6 hours in order to ensure that ketone levels decrease at the required rate of at least 0.5 mmol/l and thus guide further therapy.
- VBG every 2 hours in the first 6 hours to monitor other biochemical parameters such as pH, bicarbonate and serum potassium. (Baseline serum potassium levels must be confirmed by proper laboratory tests.)
- If a ketone-meter (to check blood ketones) is not available, the calculated anion gap helps in monitoring the patient response.
- Serial VBG monitoring should suffice as it is only 0.03 unit shigher than arterial pH. Measurement of arterial pH is required only if the patient is hypoxic or has an impaired level of consciousness,
- The bicarbonate level can be reliably used to evaluate the treatment response in the first 6 hours of management, as, subsequently, aggressive hydration using 0.9% sodium chloride could lead to the development of hyperchloraemic acidosis associated with a normal anion gap, which tends to lower the bicarbonate levels.

Fetal monitoring is very important because of several critical effects on the fetus.

- Severe maternal dehydration with acidosis may lead to reduced uteroplacental perfusion in an acidotic environment.
- Severe maternal hypokalemia could lead to fetal cardiac arrhythmias, and ultimately to fetal death.
- Fetal brain gets exposed to elevated levels of maternal 3-hydroxybutyrate and lactate, resulting in a reduced uptake of glucose by the fetal brain. These factors could heighten the risk of brain injury in the fetus and may have lasting developmental consequences.
- Fetal acidotic changes can be seen on fetal heart tracing, biophysical profile and doppler. With maternal resuscitation, the changes in the fetus are also normalised.

Decision for delivery: The fetus is to be monitored until the mother's metabolic condition is stabilized, without any immediate plan for delivery. The pregnancy can be continued until DKA is fully resolved. Nevertheless, the decision to proceed with delivery should be personalized and primarily depend on the mother's clinical condition, the fetal gestational age and the outcomes of fetal evaluations, including heart rate monitoring. A multidisciplinary approach should be employed when making this decision.

Euglycaemic Diabetic Ketoacidosis in Pregnancy

Pregnancy with ketoacidosis can present with normal or low blood glucose levels. The condition is known as Euglycaemic diabetic ketoacidosis. This can affect patients with type I diabetes, type II diabetes or gestational diabetes.

Factors that predispose to Euglycemic DKA in pregnancy:

- Maternal glucose used up by fetoplacental unit.
- Renal blood flow increases along with increased glomerular filtration of glucose; however there is no increase in tubular glucose reabsorption. This leads to glycosuria.
- Increased plasma volume during pregnancy leads to dilutional effect on blood glucose.
- Starvation is accompanied by depletion of glycogen stores and ketosis, and can thus lead to normoglycaemic DKP.

Euglycaemic DKP is managed along the same

guidelines as DKP with hyperglycemia, except it requires administration of 5% dextrose with IV saline via a separate line from the beginning of therapy. Euglycemic DKA also requires the administration of IV insulin to stop the production of ketoacids. 5% dextrose helps to prevent further hypoglycemia that may occur due to insulin administration.

Prevention of DKA in Pregnancy

Most important aspect of prevention of DKA in a pregnant woman is educating her about the precipitating factors, signs and symptoms of DKA in a simple language.

Self- monitoring of blood glucose levels, recognition of dangers signs and to seek prompt attention at their nearest healthcare facility if their blood glucose level is above 200 mg/dl, or if they have any signs of infection or any other symptoms/ precipitating factors.

Type I diabetes patients should be advised to keep a blood ketometer with them.

'Sick day' management in diabetic patients: Appropriate management of sick days in diabetic individuals is important to prevent progression to ketoacidosis. The key points include:

- Frequent monitoring of blood glucose and ketone levels every 3 hours to prevent hypoglycemia
- Modifying insulin doses, but never omitting insulin.
- Preventing dehydration
- Treating the underlying illness
- Maintaining contact with medical facility

Conclusion

Diabetic Ketoacidosis in pregnancy is a serious condition that requires prompt recognition and treatment to ensure the well-being of both mother and fetus. Management requires a multidisciplinary approach with focus on fluid resuscitation, electrolyte correction, insulin therapy and identification of precipitating factors.

Key Points

- DKA in pregnancy can occur at lower blood glucose levels than in non-pregnant individuals.
- Pregnancy induces physiological changes that increase the risk of DKA, such as reduced buffering capacity and relative insulin resistance.
- Prompt recognition and timely initiation of fluid therapy forms the cornerstone of DKA management. The management of DKA in pregnancy should involve addressing both maternal and fetal health.
- Fluid resuscitation should be initiated before insulin therapy.
- Potassium levels must be carefully monitored and corrected, as insulin can exacerbate hypokalemia.
- Identifying and educating at-risk pregnant women about DKA is the most important prevention strategy.

Suggested Reading

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ROTEM in Obstetrics- Indications and Interpretation

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Introduction

Obstetric hemorrhage is a major cause of maternal mortality in the developing world. Severe bleeding presents as a complex hemostatic disorder requiring targeted blood component therapy. Usual tests to assess hemostatic disorders such as prothrombin time (PT), activated partial thromboplastin time (aPTT), and platelet counts do not reflect the ongoing complex hemostatic changed in these scenarios, as they focus on a single step in hemostasis.

Viscoelastic hemostatic assays (VHA) are point-of-care quantitative tests with a graphical representation aiming at a global assessment of hemostasis. They have been successfully employed in trauma, cardiac surgery, and liver transplantation cases for a goal- directed therapy. They have an emerging role in obstetrics. This chapter discusses the basic principles, mechanics and interpretation of VHAs and their emerging role in the modern obstetric critical care practice.

Five Stages of Hemostasis

Hemostasis is a complex process that leads to the cessation of bleeding and the resumption of blood flow to an injured vessel. It consists of five sequential steps (Figure 1):

a. **Vasoconstriction**

b. **Platelet plug formation (primary hemostasis)** – After vascular endothelial damage, the underlying extracellular matrix (ECM) is exposed to plasma, and releases cytokines and inflammatory markers that promote platelet adhesion and aggregation at the site of the injury, including Von Willebrand Factor (VWF). The adhered platelets release thromboxane A2, serotonin, chemokines, and adenosine diphosphate and activate new platelets, which forms the primary platelet plug.

c. **Activation of extrinsic coagulation cascade**

d. **Fibrin clot formation (secondary hemostasis)**- The activation of the extrinsic coagulation cascade and the generation of fibrin clot are completed by three cellular phases of coagulation viz., initiation, amplification and propagation (Figure.1):
   - **Initiation by tissue factor (TF):** Endothelial damage exposes TF in the vascular adventitia à TF then binds to circulating VWF which also binds to platelets. TF also binds to factor VII forming an extrinsic tenase complex (ETC), which activates factor VII, IX and X à Xa binds to Va forming a prothrombinase complex (PTC), which produces small amounts of IIa (thrombin) from prothrombin. PTC remains hidden on the surface of the platelets, preventing its degradation by circulating antithrombin.1
   - **Amplification by tenase complex and propagation on activated platelets:** The small amount of IIa generated during the initiation phase activates more platelets, along with factor V, VIII, XI, and XIII à XIa activates factor IX à IIa-activated VIIIa binds to IXa to form intrinsic tenase complex (ITC), which activates factor X at a 50-fold higher rate compared to ETC to generate large amount of IIa, called as the 'Thrombin Burst' à IIa cleaves soluble fibrinogen to fibrin monomers à the fibrin monomers aggregate, cross-link (mediated by IIa-activated XIIIa) and branch to form an insoluble fibrin clot.[1]

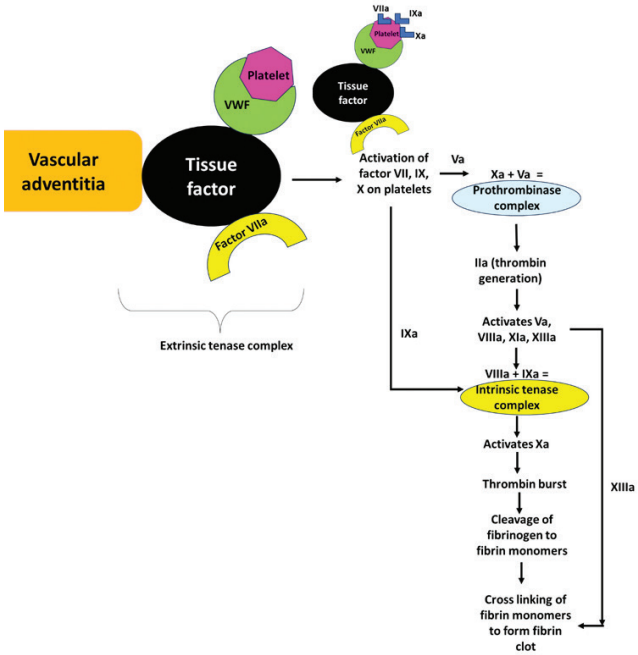


Figure 1. The Initiation, Amplification and Propagation of Extrinsic Coagulation Cascade

Notably, the intrinsic pathway is not required for hemostasis in the body. Here factor XII is activated

by anionic surfaces such as subendothelial collagen (in-vivo) or kaolin (in-vitro). Factor XIIa converts prekallikrein to kallikrein, which activates factor XII. XIIa also activates factor XI, which in turn activates factor IX. Factor IXa binds to VIIIa to form ITC, which leads to the generation of IIa, and ultimately to the formation of fibrin clot.

e. **Clot resolution (tertiary hemostasis) -** As tissue repair is completed, activated platelets contract their actin-myosin cytoskeleton, shrinking the clot. Plasminogen is converted to plasmin which promotes fibrinolysis and restores blood flow to the injured or occluded vessel. Plasminogen is activated by the tissue plasminogen activator (tPA; synthesized by endothelial cells and requires fibrin as cofactor) or by urokinase (produced by the monocytes, macrophages). The coagulation cascade is also controlled by the following mechanisms:
   - o Antithrombin, a plasma glycoprotein, works by inhibiting and cleaving factors IIa, Va and Xa. Heparin had anticoagulant effects via antithrombin action.
   - o Tissue factor pathway inhibitor (TFPI) prevents generation of Xa and IIa (during initiation phase).
   - o Protein C, S, and Z are vitamin K dependent proteins. Thrombomodulin (on endothelial cells) binds to IIa and activates protein C à activated protein C inactivates factor Va and VIIIa and prevents IIa generation. Protein Z dependent inhibitor (PZI) inhibits Xa and XIa. Protein S enhances activity of protein C and TFPI.

Pregnancy Related Changes in the Coagulation System

Pregnancy is a hypercoagulable state. There is a rise in levels of factor V, VII (up to 1000% increase), VIII, IX, X, XII, VWF, fibrinogen (twice the non-pregnant level) and plasminogen activator inhibitor 1 & 2. In contrast, levels of protein S, and tPA are reduced, while protein C levels remain unaltered. Fibrin degradation products (D-Dimer) are common in pregnant women circulation.

Standard Tests for Assessment of Hemostasis

Standard laboratory tests focus primarily on the single phase of haemostasis, with bleeding time and platelet count aimed at the formation of platelets; prothrombin time (PT), activated partial thromboplastin time (aPTT) and thrombin time assess the activation of the coagulation cascade; fibrinogen assays focus on fibrinolysis.

Viscoelastic Hemostatic Assay (VHA)

VHA is an in-vitro point-of-care test based on viscoelastic property of blood. The sample for VHA is citrated whole blood at 37^0C, which is recalcified before processing and the reports are generated within 5 to 10 minutes. The basic tests for coagulation (PT, aPTT) are performed on plasma samples requiring centrifugation, and therefore require hours to produce results. Standard coagulation tests only assess the initial phase and take hours for results generation, whereas, VHAs assess all phases of hemostasis simultaneously.

VHAs includes thromboelastography (TEG), ROTEM, and QUANTRA. The first VHA developed was TEG in 1948 at the University of Heidelberg. ROTEG system is an upgraded version of TEG that was developed in 1995-97 by Tem Innovations GmbH, Munich and later renamed as ROTEM in 2003.

The ROTEM System

In ROTEM delta, the sample undergoes automated pipetting into a cup or cuvette. ROTEM sigma system employes cartridge system instead of automated pipetting. A cylindrical pin containing an optical detector is placed into a cuvette. The pin oscillates left and right using a spring. The oscillations are detected optically and are inversely proportional to the clot firmness. A software then generates a plot of clot firmness (in millimeters) over time (in minutes) as ROTEM curve. (Figure 2) By default, the curve is plotted on both the sides of the x-axis. In contrast, the in pin the TEG system remains stationary while the cuvette rotates and because of this TEG is susceptible to vibration and mechanical shock related errors. The QUANTRA system uses acoustic or sonic radiation forces to evaluate viscoelastic properties of the blood.

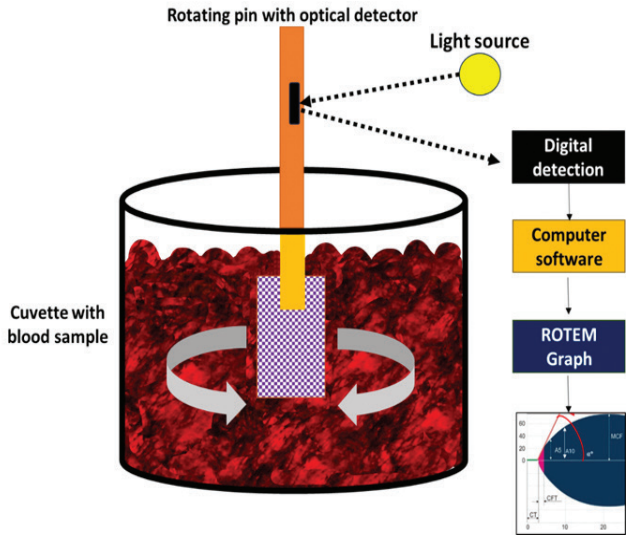
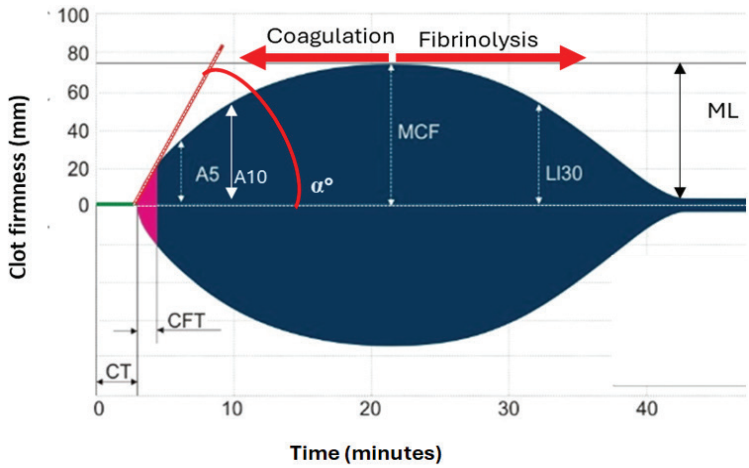


Figure 2. Mechanics of ROTEM

ROTEM generates quantitative and graphic data of hemostatic process. Table 1 and Figure 3 describe numerical parameters of ROTEM.



Abbreviations: CT, clotting time; CFT, clot formation time; A5 & A10, amplitude at 5 and 10 minutes; MCF, maximum clot firmness; ML, maximum lysis; LI30, lysis index at 30 minutes.

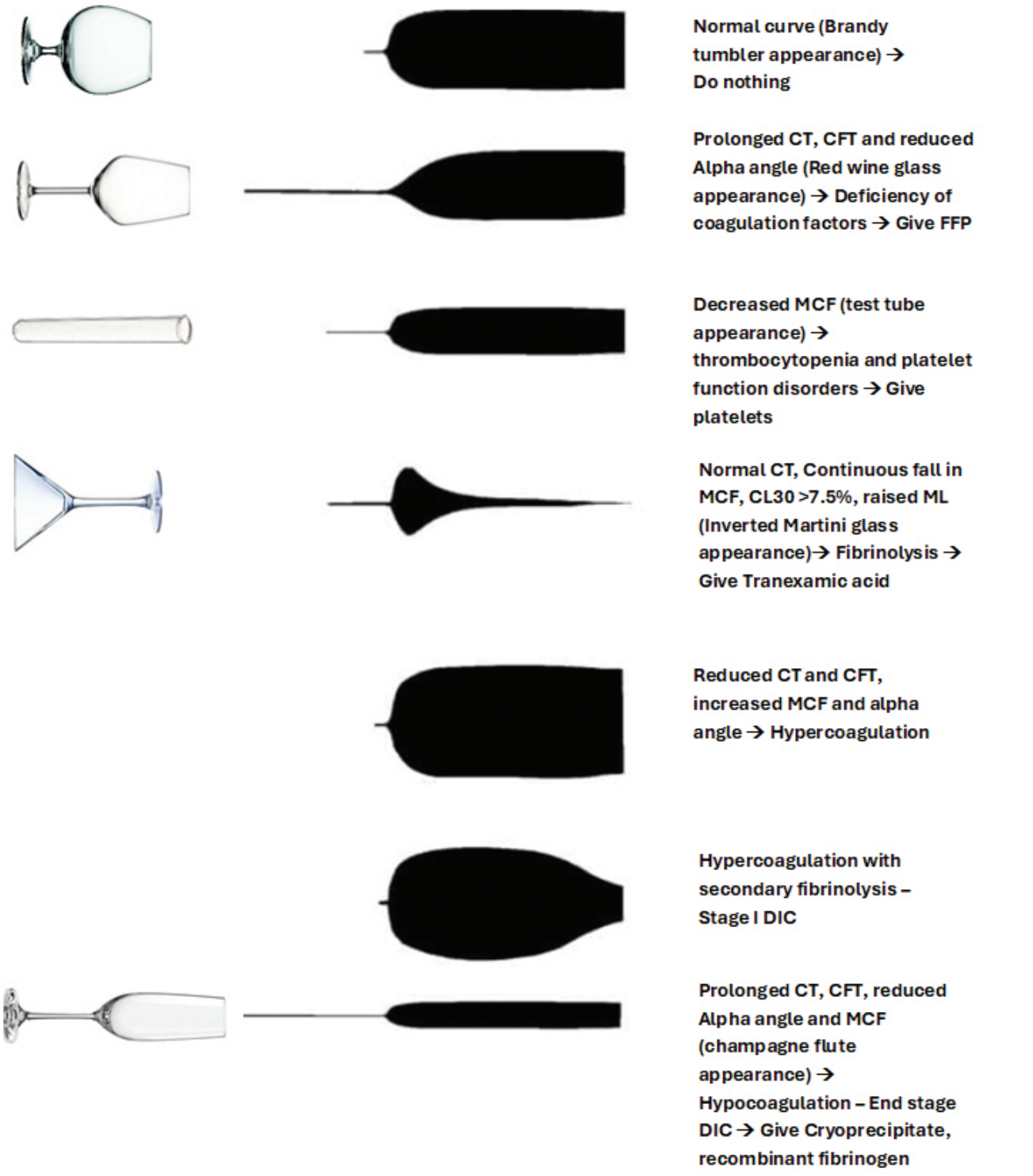
Figure 3. The ROTEM Graph

Table1. Definition, Targeted Hemostatic Steps and Clinical Relevance of ROTEM Parameters

Parameters	Definition	Steps in hemostasis	Clinical significance
Clotting Time (CT) – the initiation phase of clotting. Approximate normal value: 4 – 8 minutes	Time latency from the start of the test to the beginning of fibrin formation i.e., a waveform amplitude of 2 mm	Initiation of coagulation, thrombin generation and start of fibrin polymerization	It is dependent upon clotting factors. ↑CT à clotting factor deficiency or dysfunction/ presence of anticoagulant. ↓CTà hypercoagulability.
Clot Formation Time (CFT) – the amplification phase of clot formation Approximate normal value: 1 – 4 minutes	The time latency for the waveform amplitude to reach 20 mm from 2 mm.	Amplification of coagulation, fibrin polymerization and stabilization of fibrin clot with platelets and factor XIII	It is highly dependent on fibrinogen levels. ↑CFT à factor deficiency, platelet disorders, and hypofibrogenemia.
Alpha angle α° - the propagation phase Approximate normal value: 47^{o} - 74^{o}	The angle between the end of CT and the slope of ROTEM curve	Thrombin burst	It is highly dependent on fibrinogen levels and is a marker of clot formation. It measures the speed of fibrin formation and cross linking. ↓α° à platelet disorder, hypofibrogenemia.
Amplitude (A5, A10, A 30, A60)	The waveform amplitude (in mm) at specific time from the end of CT.		
Maximum Clot Firmness (MCF) Approximate normal value: 55 – 73 mm	The maximum waveform amplitude or the maximum clot strength. The time to reach MCF is MCF-t.	It represents overall strength of the clot and is directly proportional to fibrin polymerization, stabilization of fibrin clot with platelets and factor XIII, and hematocrit.	It is a measure of the maximum strength of fibrin clot or clot stability. MCF is largely dependent on platelets (80%), and to a lesser extent on fibrinogen (20%), and interaction of platelet and GP IIb/IIIa receptors towards clot stability. ↓MCF à platelet disorder, hypofibrogenemia.
Maximum lysis (ML)	A measure of percentage decrease in MCF at the end of the test.	Fibrinolysis	It is a measure of clot stability or lysis. If ML <15% of MCF at 60 min à stable clot If ML >15% of MCF at 60 minutes àfibrinolysis
Clot lysis index at 30 minutes (CLI30) Approximate normal value: 0 -8%	{(MCF – CF30)/ MCF} *100	CLI assesses fibrinolysis, function of fibrinolytic enzymes and inhibitors, and action of factor XIII.	An increase in CLI30 or CLI60 is suggestive of hyperfibrinolysis.
Clot lysis index at 60 minutes (CLI60)	{(MCF – CF60)/ MCF} *100		

Abbreviations: PAI-I, plasminogen activator inhibitor I; CLI, clot lysis index; MCF, maximum clot firmness; CF60, clot firmness at 60 minutes; CL, clot lysis at 30 minutes; CL, clot lysis at 60 minutes.

The gross shape of the ROTEM curve can serve as a quick guide to differentiate between bleeding caused by thrombocytopenia and bleeding secondary to clotting factor deficiency, hypofibrogenemia, or hyperfibrinolysis. (Figure 4)



Abbreviations: CT, clotting time; CFT, clot formation time; MCF, maximum clot firmness; DIC, disseminated intravascular coagulation

Figure 4. Shapes of ROTEM Graph with Hemostatic Abnormalities

Modifications of ROTEM System

The ROTEM system can simultaneously analyze four samples. Activators or additives may be added to samples for extrinsic (EXTEM) or intrinsic coagulation cascade (INTEM) activation, for fibrinogen evaluation (FIBTEM), and for the analysis of fibrinolysis (APTEM). Table.2 demonstrates different modifications of the ROTEM system. Of all modifications, the most relevant to guiding transfusion-based protocols are EXTEM and FIBTEM. When no additives are used (NATEM), the test is of doubtful clinical significance.

Table 2. Modifications of the ROTEM System

ROTEM modifications	Additives	Mechanism of action of additive	Reference range (Adults)2	Remarks
INTEM	Negatively charged surfaces (kaolin, ellagic acid, partial thromboplastin)	Activation of intrinsic coagulation cascade	CT, 100-240s CFT, 30-110s α angle, 70-83° A10: 44-66mm A20, 50-71 mm MCF, 50-72mm CLI30, 94-100% ML, <15% at 60 minutes	The parameters correspond to aPTT in a basic coagulation test. CT and CFT provide quantitative assessment of intrinsic coagulation pathway factors (XII, XI, IX, VIII, X, V, II, I), fibrin, platelet abnormality and fibrinolysis. Heparin can produce erroneous INTEM results.
EXTEM	Recombinant tissue factor, phospholipids	Activation of extrinsic coagulation cascade.	CT, 38-79s CFT, 34-159s α angle, 63-83° A10, 43-65mm A20, 50-71 mm MCF, 50-72mm LI30, 94-100% ML, <15% at 60 minutes	The parameters correspond to PT in basic coagulation assay. Factors (VII, X, V, II, I), fibrin, platelets and fibrinolysis are assessed quantitatively. EXTEM CT is shorter as compared to INTEM CT.
FIBTEM	Recalcification and Cytochalasin D	Cytochalasin inhibits the actin-myosin microfilaments in platelet and prevent platelet-mediated clot retraction.	A10, 7-23mm A20, 8-24 mm MCF, 9-25mm. Correlation of A5 with serum fibrinogen levels: • <9 mm ≈ <200 mg/dL • ≥12mm ≈ ≥250 mg/dL • ≥15mm ≈ ≥300 mg/dL	FIBTEM assays fibrinogen activity towards clot formation and stability after platelet activation. Fibrinolysis is detected earlier with FIBTEM assay as compared to EXTEM and INTEM assay. FIBTEM MCF is contributed only by plasma, while EXTEM MCF is contributed by plasma and platelets both.
APTEM	Recalcification and fibrinolysis inhibitors (aprotinin or tranexamic acid)	Aprotinin is a plasmin inhibitor	APTEM tests inhibition of fibrinolysis in the blood sample. An improvement in the APTEM assay parameters (shorter CT, raised MCF) compared to EXTEM suggests hyperfibrinolysis.	
HAPTEM (optional)	Recalcification and heparinase I or neutralase I	Heparinase degrades heparin by catalyzing cleavage of saccharide bonds.	It tests for presence of heparin in the sample. An improvement in HAPTEM parameters compared to the INTEM parameters suggests heparin activity. The ratio of INTEM CT:HAPTEM CT correlates with anti-Xa measurements in heparinized blood samples.	

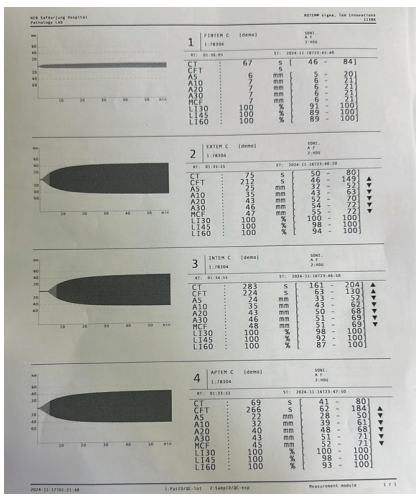
Abbreviations: CT, clotting time; CLI, clot lysis index; MCF, maximum clot firmness; CF60, clot firmness at 60 minutes; CL, clot lysis at 30 minutes; CL, clot lysis at 60 minutes; A5 A10, waveform amplitude at 5 and 10 minutes from the end of CT; PT, prothrombin time; aPTT, activated partial thromboplastin time.

ROTEM in Obstetrics

a. Hypofibrogenemia in the early stages of post-partum hemorrhage (PPH) is associated with a more severe PPH. ROTEM can detect the presence, type and severity of coagulopathy in obstetric hemorrhages and can direct specific therapy. It is proposed that goal-directed transfusion of blood components in PPH is associated with a lower rate transfusion-induced circulatory overload (TACO), a lower rate of fresh frozen plasma use and a lower rate of transfusion-related morbidity. The European Society of Anesthesiology recommends that TEG/ ROTEM be used to direct blood therapy in severe peripartum bleeding.3 In a study by Collins et al, women requiring massive blood transfusions had a median FIBTEM A5 value of 12 mm and a median serum fibrinogen level of 210 mg/dL[4,5]

Case Scenario

A 37-year-old P1L1 presented within 4 hours of vaginal delivery to the emergency department with history of severe bleeding postpartum. Her BP was 78/50 mmHg, PR 146bpm-low volume, RR 32 bpm, and SpO2 95% on room air. There was no edema/ cyanosis/ lymphadenopathy/ jaundice. Pallor was present. Bilateral chest was clear and with equal air entry. Abdomen was soft with a relaxed atonic uterus. 200 cc of clots was drained from vaginal canal. There was no cervicovaginal tear or hematoma. An immediate resuscitation was started. Oxytocics and tranexamic acid were administered; however, she continued to bleed. A trial of uterine ballon tamponade also failed. She was prepared for emergency laparotomy with 4 units each of packed RBCs, platelet rich plasma and fresh frozen plasma. Systematic devascularization was performed however, she continued to bleed. As an intervention of last resort, a decision for hysterectomy was taken. Continuous oozing from stump was observed intraoperatively. A ROTEM was performed.



Q. Describe the hemostatic abnormality

The hemostatic abnormalities are hypofibrogenemia (FIBTEM A5 ↓, EXTEM CFT ↑, MCF ↓), factor deficiency (EXTEM CFT ↑), platelet disorder (EXTEM CFT ↑, MCF↓), and minor degree of hyperfibrinolysis (APTEM CT ↓ compared to EXTEM CT, however, MCF largely unchanged).

Q.What therapy can be administered to correct the disorder?

The patient needs fibrinogen replacement in form of cryoprecipitate or human fibrinogen concentrate. She also needs fresh frozen plasma and platelets.

Second dose of tranexamic acid can be repeated.

Drotarova et al have given ROTEM-guided transfusion protocol in adults as described in Table.3.

Table 3. Replacement Criteria for Blood Transfusion According to ROTEM Parameters

EXTEM
• CT >80 s à PCC, FFP
• α angle <63° à Fibrinogen concentrate*/cryotherapy
• MCF <45 mmà Fibrinogen concentrate*/cryotherapy and platelets
• CL30/60 <82% or ML >15%à Tranexamic acid
FIBTEM
• A5 <9mm àFibrinogen concentrate*/cryotherapy (1st target A10 is ≥12 mm; 2nd target A10 is ≥15 mm).
• FIBTEM A10 <7 mm
• FIBTEM MCF ≤9mm with EXTEM MCF <45mm à Fibrinogen concentrate*/cryotherapy
ROTEM sigma FIBTEM A5 has better correlation with Clauss's method of fibrinogen assessment compared to ROTEM delta.

Abbreviations: CT, clotting time; PCC, prothrombin concentrate complex; FFP, Fresh frozen plasma; MCF, maximum clot firmness; CL30 60, clot lysis at 30 and 60 minutes; MCF, maximum clot firmness; A5, waveform amplitude at 5 minutes from the end of CT.

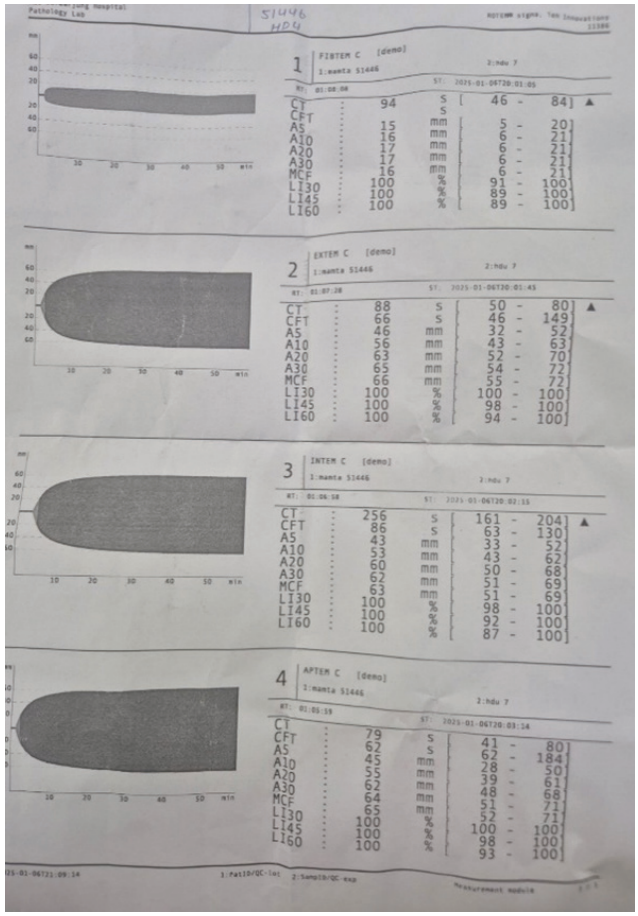
*Fibrinogen concentrate dose (g) = (target FIBTEM MCF (mm) – actual FIBTEM MCF (mm)) × (body weight (kg)/70) × 0.5 g/mm.

One unit (10-20 mL) of cryoprecipitate has 150-300 mg of fibrinogen (15g/L) and increases plasma fibrinogen levels by 5-10 mg/dL. The standard adult dose is one pool of 10 units of cryoprecipitate. Apart from fibrinogen, cryoprecipitate contains factor VIII, VWF, and factor XIII.

One unit of 300 mL of FFP contains about 500 mg of fibrinogen and increases serum fibrinogen levels by 15-25 mg/dL. The recommended FFP dose is 12-15 mL/Kg (at least 10 mL/Kg). FFP also contains all clotting factors, including 0.7 IU/mL of factor VIII, albumin and immunoglobulins.

One vial of fibrinogen concentrate (Fibrogen-I) contains 1 g of lyophilized human fibrinogen and increases serum fibrinogen levels by 30 mg/dL.

Fibrinogen concentrate dose (g) was calculated as follows: {(12 – 7)*50/70}*0.5 = 1.78g ≈ 2g, hence 2 vials (2 g) of Fibrogen-I were administered to her. Post therapy, ROTEM showed remarkable improvement in hemostasis.



Non-dilutional acquired coagulopathy is often seen during pregnancy complicated by acute fatty liver of pregnancy, hemolysis elevated liver enzymes and low platelet (HELLP) syndrome, placental abruption, amniotic fluid embolism, intrauterine demise and disseminated intravascular coagulation. ROTEM can be used to guide coagulopathy management in these cases.6 Figure.4.

Table 4 describes trends in ROTEM parameters with obstetric coagulopathies.

b. Pregnant hemophilia carriers may benefit from the INTEM assay to guide predelivery therapy with recombinant factor VIIa.

Table 4. Trends in ROTEM Parameters with Obstetric Conditions Affecting Hemostasis

Obstetric condition	ROTEM parameter
Gestational thrombocytopenia, immune-mediated thrombocytopenia (quantitative platelet disorder)	EXTEM ↓ MCF
Preeclampsia (quantitative and qualitative platelet disorder; increased thrombin generation)	EXTEM ↑CT, ↑CFT EXTEM ↓ MCF
Acute fatty liver of pregnancy	EXTEM ↑ CT, ↑CFT, ↓MCF INTEM ↑CT, ↑CFT, ↓MCF
HELLP syndrome	Similar to acute fatty liver plus FIBTEM ↓ MCF
Amniotic fluid embolism, abruption, DIC (Complex consumptive coagulopathy)	EXTEM ↓MCF, ↑CT, ↑CFT INTEM ↓MCF, ↑CT, ↑CFT FIBTEM ↓MCF, ↑CT, ↑CFT APTEM ↓MCF (with hyperfibrinolysis), ↑CFT HEPTEM ↑CT (with endogenous heparinization)
Anticoagulation with heparin	INTEM ↑CT, ↑CFT HAPTEM ↑CT, ↑CFT NATEM ↑CT, ↑CFT

Abbreviations: HELLP syndrome, hemolysis elevated liver enzymes, low platelet counts; DIC, disseminated intravascular coagulation; CT, clotting time; CFT, clot formation time; MCF, maximum clot firmness

Limitations of ROTEM

ROTEM has limited availability, has a high inter-operative variability. Skilled manpower is needed to perform the test. Result interpretation has long learning curve.

ROTEM and other VHAs have not reported to be beneficial in Von Willebrand Disease and it is recommended that ROTEM is not used as a substitute for the standard tests (factor VIII and VWF assays).

Although EXTEM and FIBTEM MCF are beneficial in the prediction of platelet disorders and bleeding risk in non-obstetric patients, their role in gestational thrombocytopenia and immune-mediated thrombocytopenia is not well known. Similarly, the use of ROTEM/TEG to detect platelet dysfunction in preeclampsia is unknown.

ROTEM has limited ability to evaluate anti-Xa activity in patients receiving LMWH for venous

thromboprophylaxis. This is because the additive, heparinase, is not an effective neutralizer of LMWH.

VHAs require testing of samples at 37°C. This means that it is not effective in assessing the effects of hypothermia on coagulation. Moreover, in-vitro tests do not take into account the dynamics of blood flow and the in-vivo stress on clot formation.

VHAs are also not effective in the evaluation of substances that modify the adhesion of platelets.

Despite the proposed beneficial effects of ROTEM assays in guiding blood transfusions in obstetric patients, the optimal threshold for a TEG/ROTEM parameter is unknown.6 There are no prospective randomized controlled trials comparing the efficacy of VHAs with empirical or conventional transfusion approaches in obstetrics. Because of insufficient evidence, NICE does not recommend the routine use of VHA for detection, treatment and monitoring of hemostasis in postpartum hemorrhage.[7]

Conclusion

ROTEM is a global hemostasis assessment test which has shown benefits in guiding goal-directed transfusions in liver transplantation and cardiac surgery. Its role in guiding targeted therapy in obstetric hemorrhages and non-dilutional obstetric coagulopathies appears promising. Adequately powered randomized controlled trials are required to validate such findings.

Suggested Reading

1. Park S, Park JK. Back to basics: the coagulation pathway. Blood Res. 2024 Oct 28;59(1):35.
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4. Collins PW, Lilley G, Bruynseels D, Laurent DB, Cannings-John R, Precious E, et al. Fibrin-based clot formation as an early and rapid biomarker for progression of postpartum hemorrhage: a prospective study. Blood. 2014 Sep 11;124(11):1727-36.
5. Collins PW, Cannings-John R, Bruynseels D, Mallaiah S, Dick J, Elton C, Weeks AD, et al. Viscoelastometric-guided early fibrinogen concentrate replacement during postpartum haemorrhage: OBS2, a double-blind randomized controlled trial. Br J Anaesth. 2017 Sep 1;119(3):411-421.
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Role of Point of care USG (POCUS) in Maternal Collapse

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Introduction

As ultrasound technology has improved in quality and decreased in footprint, it is becoming more useful in the routine care of critically ill patients and an excellent tool for both, diagnosis and hemodynamic monitoring. During the past decade, the application and utilization of point-of-care ultrasound (POCUS) have skyrocketed. Following appropriate training and governance, POCUS can provide timely and critical information. Awareness of a few basic POCUS measurements is useful for assessment of any hemodynamically unstable patient. Moreover, visual information can be obtained quickly at the bedside without the risk of ionizing radiation.

A global POCUS physical examination of patients in shock can determine fundamental hemodynamic measures (e.g., stroke volume, cardiac contractility, and valvular diseases). For the purposes of hemodynamic monitoring, the basic transthoracic echocardiogram provides a wealth of information in experienced hands and offers minimal risk to the patient. In addition, POCUS can assess organ congestion and fluid tolerance.

Lung ultrasonography allows estimation of both extravascular lung water and fluid collections in the pleural space. Therefore, a thorough evaluation of lung and cardiac ultrasonography among patients with respiratory failure can lead to a narrower differential diagnosis.

Various roles of Point of care Ultrasound (POCUS) in Maternal collapse are as -

- Obstetrical Diagnosis
- Heart And Lung USG
- Dynamic Monitoring by IVC Compressibility For Fluid Responsiveness
- Abdominal and thoracic cavity - eFAST
- Pulmonary Embolism, DVT
- RUSH Protocol
- BLUE Protocol

Apart from application of bedside Ultrasound for Obstetrics diagnosis, POCUS can also be utilized for diagnosis of etiology of shock. Shock is a state of circulatory dysfunction causing reduced tissue perfusion and metabolic upset. It is commonly encountered in the maternal collapse and maternal mortality. Diagnosing the etiology of shock in a patient can be challenging, as many causes share a similar clinical picture. A recent study has shown adding point-of-care ultrasound (POCUS) to the clinical assessment increases diagnostic accuracy for the etiology of shock from 45% to 89%. Another study showed early use of POCUS in patients with hypotension accurately guided diagnosis, significantly reduced diagnostic uncertainty, and substantially changed management and resource utilization in the emergency conditions.

"Rapid Ultrasound for Shock and Hypotension" RUSH Protocol

The RUSH Protocol was published in 2009 by Perera et al. It was designed to be a rapid and easy-to-perform US protocol (<2 minutes) for emergency physicians. It is helpful to diagnose cause of undifferentiated shock in a rapid but systematic manner as shown in Table 1.

The components of the RUSH protocol include examination using mneumonic "HI-MAP."

1. Heart
2. Inferior vena cava
3. Morrison's pouch / Fast abdominal views with thoracic windows
4. Aorta

5. Pneumothorax Screening

RUSH Examination

- The RUSH protocol involves a 3-step bedside using probe position as in Figure 1 and aids in physiologic assessment of -

  Step 1: How is the pump (Heart – Look for pericardial effusion/ Tamponade/ LV Contractility and RV Strain)

  Step 2: How full is the tank? Is the tank leaking or compromised? (Fullness of Inferior vena cava, thoracic and abdominal compartments- eFAST exam (Ectopic) and Lung exam)

  Step 3: How are the pipes? (Large Arteries/Veins for DVT)

Table 1: RUSH Protocol for Diagnosis of Shock

Rush Evaluation	Hypovolemic shock	Cardiogenic Shock	Obstructive Shock	Distributive Shock
Pump	Hyper-contractile heart Small Chamber size	Hypo contractile heart Dilated heart	Hyper-contractile heart Pericardial Effusion Cardiac Tamponade RV Strain Cardiac thrombus	Hyper-contractile heart (Early sepsis) Hypo contractile heart (Late sepsis)
Tank	Flat IVC Flat jugular veins Peritoneal fluid (Fluid loss) Pleural fluid (Fluid loss	Distended IVC Distended jugular veins Pulmonary edema Pleural fluid (effusion) Peritoneal fluid (ascites	Distended IVC Distended Jugular veins Absent lung sliding (pneumothorax)	Normal or small IVC (early sepsis Peritoneal fluid (peritonitis Pleural fluid (empyema)
Pipes	Abdominal aneurysm Aortic dissection	Normal	DVT	DVT Normal
DVT - Deep venous thrombosis, IVC - Inferior vena cava, RV - Right Ventrcle				

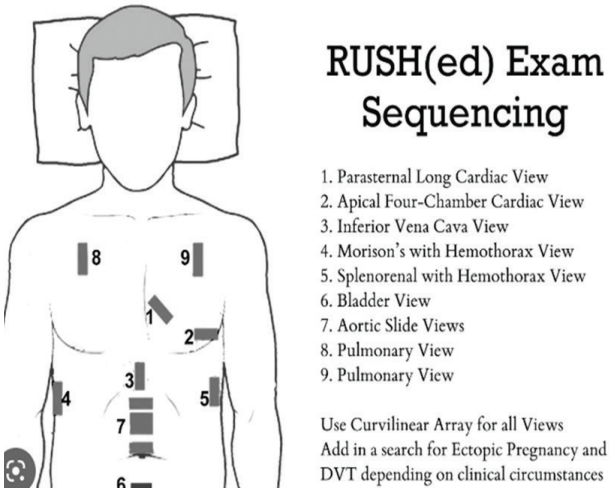

Figure 1: Probe position for RUSH Exam in Critically sick patient

Step 1: Examination of the Pump

- **Views:** Parasternal long and short axis views, apical 4-chamber view and sub xiphoid 4-chamber view
- **Probe:** Phased array probe (3.5 – 5 MHz)

1. Parasternal Long Axis View (PLAX)

Transducer position should be at left sternal edge 2nd – 4th intercostal space. Maker dot direction points towards the right shoulder (Figure 2 & 3)

2. Parasternal Short Axis View (PSAX)

Transducer position should be at left sternal edge; 2nd – 4th intercostal space. Marker dot direction points towards left shoulder (90 degree clockwise from PLAX view). By tilting transducer on an axis between the left hip and right shoulder, short axis views are obtained at different levels, from the aorta to the LV apex. (Figure 2 & 4)

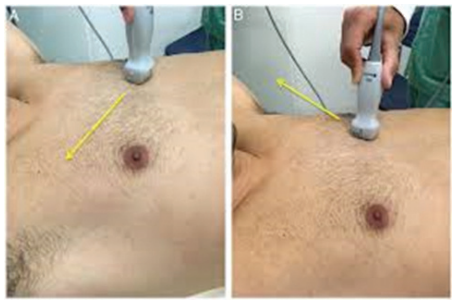

Figure 2: Probe position for PLAX and PSAX view

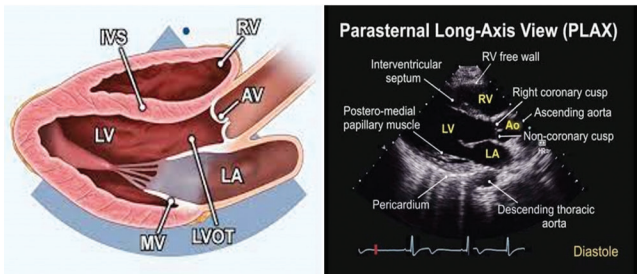

Figure 3: Parasternal Long-Axis View (LA-Left Atria, LV-Left Ventricle, RV-Right Ventricle, AV- Aortic Valve, IVS-Inter Ventricular Septum, MV-Mitral Valve, LVOT-Left Ventricular Outlet Tract)

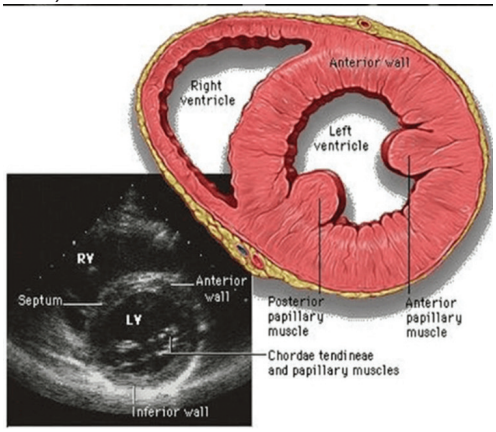

Figure 4: Parasternal Short Axis View

3. Apical Four Chamber View

TRANSDUCER POSITION: The probe is placed lateral to the nipple line in the 5th intercostal space near the anterior axillary line with the pointer facing toward the left axilla. (Fig 5)

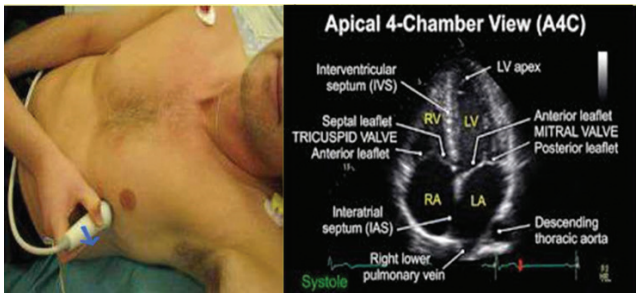

Figure 5: Probe placement and overview of Apical Four Chamber View

4. Subxiphoid view

Transducer position - probe is held as parallel to abdominal wall as possible and Probe marker is placed toward the left side in the direction of left shoulder as in figure 6.

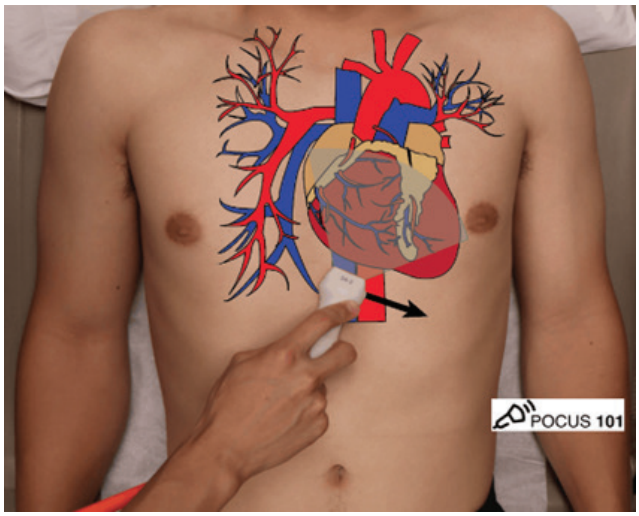

Figure 6: Probe placement and overview of Subxiphoid View

Abnormal Findings are

A. Pericardial Effusion and potential Cardiac tamponade

- Findings: Pericardial effusions are best identified posterior to left ventricle and anterior to descending aorta as in Figure 7.
- Also look for collapse of right ventricle during diastole (indicates tamponade effect).

B. Assessment of Right ventricular strain

- Findings: An enlarged RV indicates right ventricular failure as one of the causes of shock. In an acute setting, it may indicate an acute pulmonary embolism or acute RV infarction. Normally, the RV is < 60% the size of LV. When RV equals or is more than LV, suspect RV failure.(Fig 8)

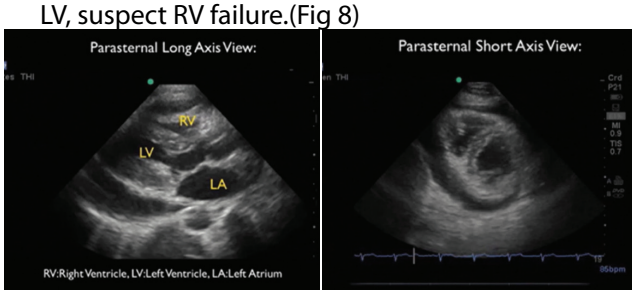

Figure 7: PLAX and PSAX View showing Pericardial Effusion

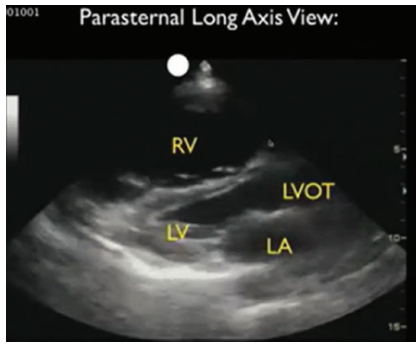

Figure 8: PLAX View showing Right ventricular strain

- Mc Connel's sign: RV free wall hypokinesia with sparing of the apex. It has specificity of 96% for pulmonary embolism, but sensitivity is only 16%.

C. Evaluation of Left ventricular Contractility.

- Findings: Normally, the anterior leaflet of mitral valve touches the septum. If it does not, it may indicate poor ventricular contractility.
- A vigorously contracting ventricle will almost completely obliterate the ventricular cavity during systole. <30% difference of LV size between systole and diastole indicates severely decreased LV function.

Step 2: Examination of the Tank

A. Inferior vena cava

- It is viewed in sub-xiphoid position using phased array probe (3.5 – 5 MHz). Optimize the ultrasound image and zoom in if you need to.
- With your calipers, try to measure its diameter approximately 2 cm from its attachment point to the right atrium.
- If you are using M mode, then it is at this spot that you want to place your cursor and then take measurement of IVC at Max and Min. Regardless of whether you are using 2D measurements or M mode, make sure you are measuring it when it is at it's widest diameter.
- Findings: A smaller caliber IVC (<2 cm diameter) with

an inspiratory collapse greater than 50% roughly correlates to a CVP of less than 10 cm of water and may indicate a hypovolemic or distributive shock.

- A larger sized IVC (>2 cm diameter) that collapses less than 50% with inspiration correlates to a CVP of more than 10 cm of water and may indicate a cardiogenic or obstructive shock.
- Relationship between IVC size and CVP with normal respiration is given in the table below-

Table 2. Relationship between IVC size and CVP with normal respiration

IVC Size (cm)	Respiratory change	CVP (cm H_2O)
< 1.5	Total collapse	0 – 5
1.5 – 2.5	>50 % collapse	6 – 10
1.5 – 2.5	<50 % collapse	11 – 15
>2.5	<50 % collapse	16 – 20
>2.5	No change	>20

- **Caval Index is the IVC** collapsibility index in spontaneous breathing patients, is calculated by the difference between the maximum (expiratory) and minimum (inspiratory) IVC diameters, divided by the maximum IVC diameter, and presented as a percentage. In a volume depletion status, where the IVC is collapsed, the index will be higher, approaching 100% as opposed to a state of volume overload, where the IVC is distended, therefore the caval index is very low, approaching 0%.

$$\text{Caval index} = \frac{\text{Maximum diameter of IVC (expiratory)- Minimum diameter (inspiration)x 100}}{\text{Maximum diameter of IVC (expiratory)}}$$

Using this formula, the cut off is 18% change. Values > 18 % predict an increase in cardiac output to fluid challenge.

This relationship is reversed with positive pressure ventilation, in which positive intrathoracic pressure accompanies inspiration. In mechanically ventilated patients, IVC distensibility > 18% was proved as a predictor of fluid responsiveness.

Distensibility Index (DI) = [Maximum diameter (Inspiration) - Minimum diameter (Expiration)]/ Minimum diameter (inspiratory)

The degree of respiratory variation is related to volume status and venous return (Figure 9). Some exceptions should be noted, such as the plethoric IVC that may be found in cardiac tamponade, when the patient could be normo-volemic or hypovolemic despite an indication of volume overload by an IVC ultrasound assessment. Therefore, findings should always be interpreted within their clinical context or after integration with a cardiac evaluation.

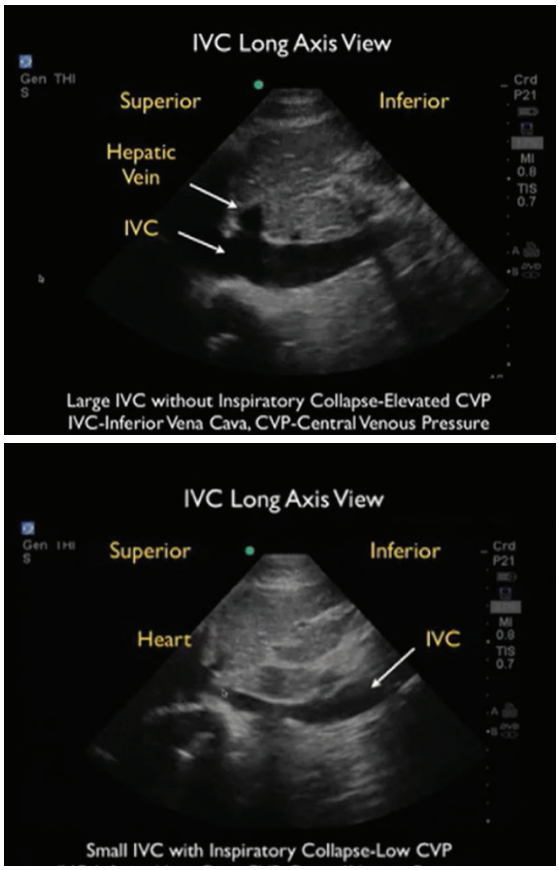

Figure 9: IVC Long Axis View showing Elevated and Low Central Venous Pressure (CVP)

- The internal jugular veins can also be examined to evaluate the intravascular volume. Veins that are distended, with a closing meniscus level that is high in the course of the neck, suggest a higher CVP.

B. Abdominal cavity

- The abdominal FAST views are used to visualize the peritoneal cavity using phased array probe (Figure 10).

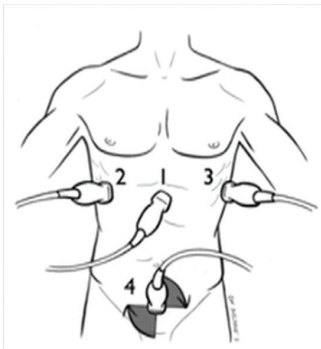

Figure 10: Probe position for Abdominal FAST View 1. Cardiac subxiphoid view, 2. Right Upper quadrant - hepatorenal view, 3. Left Upper quadrant - Splenorenal view and 4. Suprapubic view.

- Specific views include the hepatorenal space or Morison's pouch, the perisplenic space, and the recto vesicular / rectovaginal space or pouch of Douglas.(Fig 11)

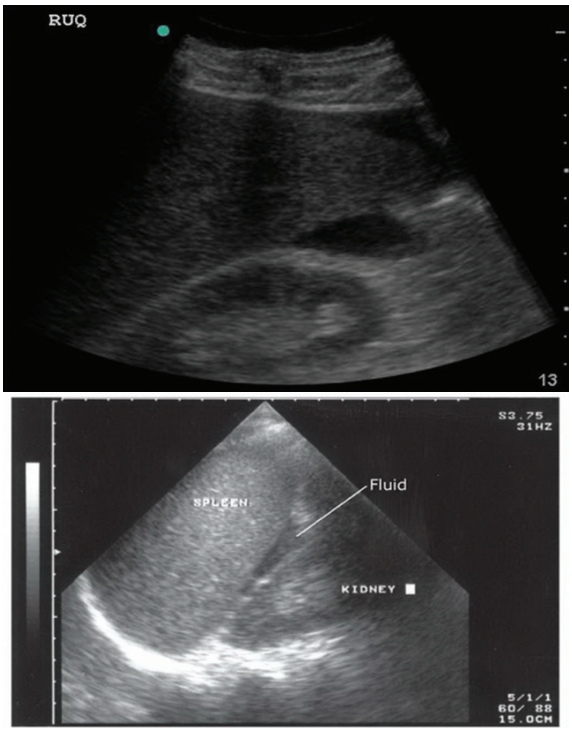

Figure 11: Right Upper quadrant - hepatorenal view showing fluid in Morrison pouch, 3. Left Upper quadrant – Splenorenal view showing fluid in splenorenal region.

- Findings: free fluid noted in these potential spaces could indicate a hypovolemic shock due to internal blood loss, fluid extravasation, or other pathologic fluid collections.

C. Thoracic cavity

- Evaluation of the thoracic cavity is done by extended FAST or E-FAST views by including views of the thoracic cavity with the abdominal FAST examination.
- Findings: Aiming the probe above the diaphragm will allow for identification of a thoracic fluid collection, which may indicate a hemothorax. (Fig 12)

D. Intrathoracic compromise

- Probe: Linear probe (7.5 – 10 MHz)
- Location: Midclavicular line, 3rd – 5th intercostal space
- Findings:

Emergency ultrasound has proved to be more sensitive than clinical examination and Chest x ray for the diagnosis of lung pathologies.

In normal aerated lung, along with normal sliding sign, hyperechoic, horizontal lines arising at regular intervals from the pleural line can be seen, which are called A-lines (Fig 14). In short, if you see A-lines, the lungs are filled with air. B-lines are defined as discrete laser-like vertical hyperechoic artifacts that arise from the pleural line and extend to the bottom of the screen without fading, move synchronously with lung sliding and erase A-lines (Fig 13).

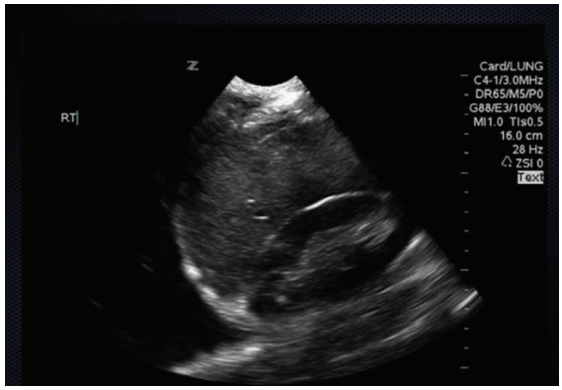

Figure 12: Right upper quadrant view extended to thoracic cavity showing fluid in pleural space (Thoracic spine sign)

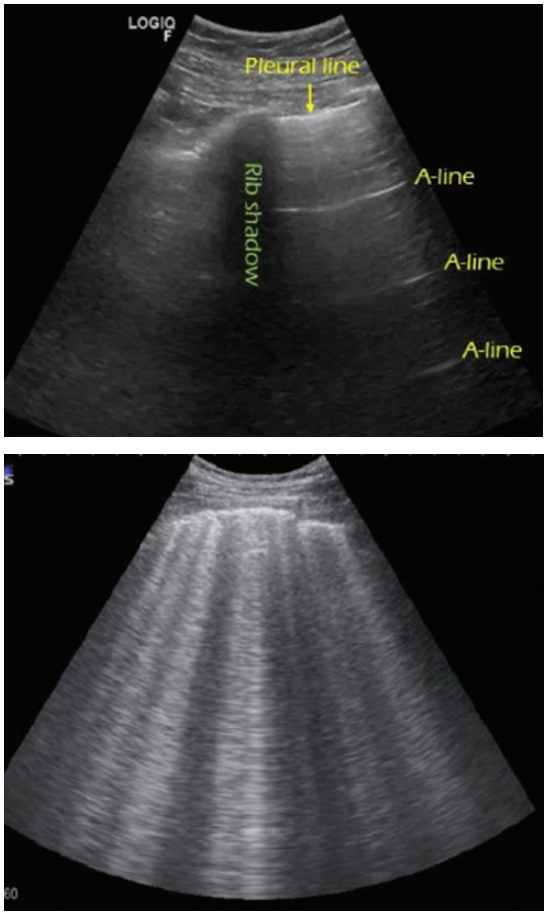

Figure 13: USG Lung showing Normal lung shadows with A lines (Left) and Multiple B lines suggesting Pulmonary congestion (Right)

Pulmonary congestion

Alveolo-interstitial syndrome (AIS), which is presence of multiple B-lines arising from the pleural line. B-lines seen on lung ultrasound provide semi-quantitative estimation of extravascular lung water, which is particularly important in critically ill patients and those with cardiorenal syndrome.

Pneumothorax - Absent lung sliding and absent comet tails, Stratosphere sign and Bar-code sign on M mode and presence of "lung point".

Step 3: Examination of the Pipes

A. Aorta

- Probe: Phased array probe (3.5 – 5 MHz)
- Location: Longitudinal and transverse views of abdominal aorta at 4 levels (infracardiac, suprarenal, infrarenal, and at the iliac bifurcation) plus PLAX and suprasternal views
- Findings: Aortic size >3 cm indicates abdominal aortic aneurysm (AAA). If >5 cm, consider ruptured AAA if no other cause for hypotension is found
- An aortic dissection may be indicated by a dilated proximal aortic root (>3.8 cm) in the PLAX view or the presence of an intimal flap anywhere along the course of the aorta
- A suprasternal view with the phased array probe helps to visualize the arch of aorta

B. Large Veins

- Probe: Linear probe (7.5 – 10 MHz)
- View: Large veins of the lower limb at 2 sites

a. The proximal femoral vein just below the inguinal ligament

b. The popliteal vein along the popliteal fossa
   - Findings: Mass in the lumen of the vein is suggestive of deep vein thrombosis (DVT).
   - The pathognomonic finding of DVT will be incomplete compression of the anterior and posterior walls of the vein. (Fig 14)

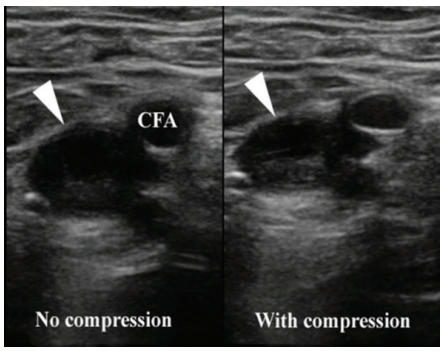

Figure 14: USG lower limb incomplete compression test suggestive of DVT.

Other utility of POCUS includes

Optic Nerve Sheath Diameter (ONSD)

Bedside ocular ultrasonography for measuring ONSD can be used an early test for diagnosing raised ICP as it is a noninvasive, cost-effective bedside test, which can be repeated for re-evaluation. It is measured in supine position using 10 MHz linear array probe on closed eyelid. ONSD was measured 3 mm behind the globe in each eye. A mean binocular ONSD > 5 mm is 100% sensitive for elevated Intra Cranial Pressure. (Figure 15)

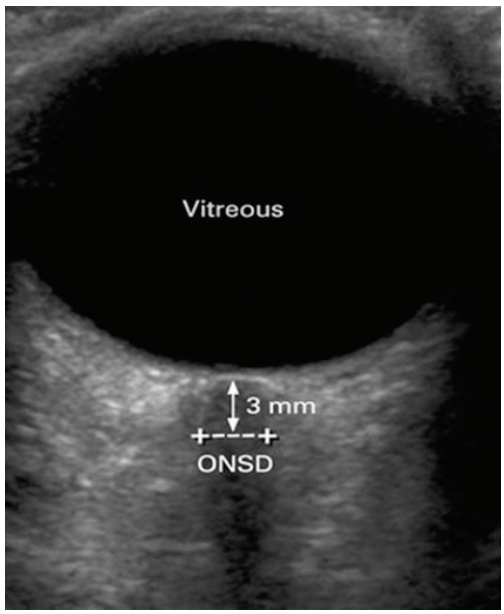

Figure 15: Showing ONSD measurement on Ocular USG

Conclusion

POCUS has been a practice-changing technology for the care of the emergent and critically ill patient. The ability to look inside the human body in real time without the risk of radiation helps physicians narrow the differential diagnoses early on in a patient's evaluation and helps guide decisions regarding further testing (if any is indicated). Furthermore, POCUS, ultimately improve initial diagnostic accuracy, initiation of proper management, and thus overall patient care. As the technology becomes more accessible, we can expect it to diffuse broadly.

Suggested Reading

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Approach to Acid-Based Disorders

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Introduction

Acid-based disturbances are commonly encountered in critically ill patients in ICUs and result from a wide variety of metabolic and respiratory disorders. Besides, information about the seriousness of the underlying diseases, acid-based disturbances have significant hemodynamic and other physiological effects. So an early diagnosis and treatment of these disturbances is an important component of the management of critically-ill patients. This requires a systematic approach to interpretation of blood gases and simultaneously measured electrolytes. Arterial blood gases is point of care test which gives important information about the oxygenation (pO_2), ventilation (pCO_2), acid base status (bicarbonates) and other important information such as electrolytes.

Acid-Base Physiology

The acid-based status of the body is normally kept within the narrow range of pH despite the daily production of large amount of acid, as a result of various metabolic activities. Approximate 12000–15000 mEq of volatile acids in the form of CO2 are generated each day and excreted by the lungs and about 1 mEq/kg/day of non-volatile acids (mostly phosphoric and sulfuric acid) are produced daily and excreted by the kidney.

The pH of the body fluids is determined by the:

- Amount of acid produced
- The ability of the lungs and kidney to excrete the acid load
- The buffering capacity of the blood.

If an extra acid or base is introduced, the body tends to mitigate the change in pH through the action of multiple buffers and activation of compensatory mechanisms. A buffer is a substance that can either absorb or donate protons to a solution.

The important extracellular buffers at physiologically relevant pH are:

- Bicarbonate (HCO_3– + H+ « H_2Co3 « H_2O + CO_2);
- Plasma proteins (protein- + H+ « H-proteins);
- Hemoglobin (Hgb– +H+ « H-hgb); and
- Phosphates (HPO_{42}– + H+ « H_2Po_4–).

The principal buffering system for non-carbonic acid in the extracellular fluid is the carbonic acid–bicarbonate pair. It is not necessary to measure each buffer separately, because all buffers behave as if they are in functional contact with a common pool of [H+] and any alteration in [H+] results in equal changes in the ratio of each buffer. This is also termed as isohydric principle.

So, clinically when we assess a patient's acid–base status we evaluate the carbonic acid bicarbonate system, since it is easily measured.

The pCO_2 – HCO_3, buffer system is reflected in the following formula.

CO_2 gas ®CO_2 (dissolved) + H_2O « H_2CO_3 « $H^+ + HCO_3^-$

The relation of pH to this buffering system is expressed by the Henderson–Hasselbalch equation:

$pH = pK + Log\ (HCO_3)/H_2CO_2$

Carbonic acid is present in blood in such small quantities that it is unmeasurable, but because carbonic acid is in equilibrium with the CO_2 in solution and the dissolved CO_2 depends on the pCO_2 in the arterial blood, the carbonic acid term of the equation can be replaced by the term pCO_2 times the solubility coefficient (0.03).

Thus, the Henderson–Hasselbalch equation can be rewritten as:

$pH = pK + Log\ HCO_3/(0.03) \times pCO_2$ = Kidny/Lung = Metabolic/Respiratory

$7.4 = 6.1 + 24/(0.03) \times 40$

Thus, the pH is determined by the ratio of the serum bicarbonate concentration to the partial pressure of CO_2 in the arterial blood. The bicarbonate concentration is regulated by the kidneys and the pCO_2 is regulated by the lungs.

The interrelation of $[H^+]$, pCO_2 and $[HCO_3^-]$ can also be illustrated by the Henderson equation

$(H^+) = 24 \times pCO_2/(HCO_3^-)$

This equation is helpful as a bedside tool to predict or evaluate the accuracy, in other terms the internal consistency of the three acid-based parameters.

The $[H^+]$ can be calculated from the pH given that a pH of 7.4 equals a $[H^+]$ concentration of 40 nEq and there is a linear and inverse relationship between pH and $[H^+]$, between the pH of 7.1 and 7.5. For every 0.01 change in

pH, there is a 1 neq/L change in the [H^+] concentration. When the reported HCO_3^- concentration and pCO_2 are entered into the right side of the equation, the equation should solve to equal the [H^+] predicted by the arterial pH. If it does not, then one of the reported values is wrong.

Terminology of Acid Base Disorders

The acidity of body fluid is measured in terms of hydrogen ion concentration [H+] and expressed as pH, which is the negative log of the [H+]. The normal pH varies between 7.36 and 7.44 with an average of 7.4, which corresponds with the [H+] concentration of 40 nano equivalent/L (nEq/L). There is an inverse relationship between pH and [H+] concentration, i.e. as the pH rises the hydrogen ion concentration falls and vice versa. This relationship is curvilinear with the linear component falling between the pH of 7.1 and 7.5. In this range, 0.01 unit change in pH from 7.40 will change the [H+] by roughly 1 nEq/L. However when we consider the entire curvilinear range, [H+] changes by 1.25 per 0.01 pH unit decrement or 0.8 per 0.01 pH unit increment from 40 nEq/L When pH changes by 0.3 log units, the corresponding [H+] in whole number doubles or halves.

- Acidosis is a pathophysiological process that tends to acidify body fluids [lower plasma (HCO3–), or increase in PaCO2] and if unopposed will lead to a decrease in pH
- Acidemia is defined as increase in absolute (H+) and fall in pH below 7.36
- Alkalosis is a pathophysiological process that tends to alkalinize body fluids [raise plasma (HCO3–), or lower PaCO2] and if unopposed will lead to increase in pH
- Alkalemia is defined as decrease in [H+] and a rise in pH above 7.44.

Simple acid-base disorders

As already mentioned, the pH of a solution is determined by the ratio of HCO_3^- and pCO_2. The pathologic processes that primarily change the bicarbonate levels are referred to as metabolic disorders and pathologic processes that primarily alter the CO_2 levels in blood are referred to as respiratory disorders.

- Metabolic acidosis: Primary decrease in bicarbonate levels
- Metabolic alkalosis: Primary increase in the bicarbonate levels
- Acute respiratory alkalosis: Primary decrease in the CO_2 levels without adequate metabolic compensation
- Chronic respiratory alkalosis: Primary decrease in the CO2 levels with adequate metabolic compensation
- Acute respiratory Acidosis: Primary increase in the CO_2 levels without adequate metabolic compensation
- Chronic respiratory acidosis: Primary increase in the CO_2 levels with adequate metabolic compensation.

Normal ABG values in pregnancy: The normal values *of pH, $PaCO_2$, and PaO_2 during pregnancy are 7.40-7.46, 28 mm Hg and 105 (sitting), 95 (supine) mmHg respectively, instead of 7.35-7.45, 40 mm Hg and 100 mm Hg in otherwise healthy individuals*. These values should be taken as baseline while interpreting acidemia, respiratory acidosis and alkalosis and when calculating the adequate respiratory compensation for various metabolic acid-based disorders as seen in Table 1.

Table 1: Normal Values of Blood Gases in Pregnant and Non Pregnant

Parameter	Non pregnant	Pregnant
PH	7.35-7.45	7.40-7.46
PCO_2	35-45 mmHg	27-34 mmHg
PO_2	80-100 mmHg	95-105mmHg
HCO_3	22-26	18-21
SPO_2	93-100%	95-100%

Compensatory Response: In each of the four primary disorders, the initial process not only alters acid-based equilibrium directly but sets in motion secondary compensatory responses that changes the other component of the pCO_2–Bicarbonate pair, to bring the ratio of HCO_3– to pCO_2 back towards normal and thus helps normalize the pH.

In metabolic acidosis, the primary disturbance is fall in the HCO_3– level, the body to return the pH back to normal induces a fall in pCO_2 via hyperventilation. Similarly, in metabolic alkalosis the primary increase in bicarbonate is compensated for by a decrease in ventilation and increase in pCO_2. In respiratory acidosis, the compensatory response is a rise in HCO_3– due to decreased renal excretion of HCO_3–. The compensatory responses have following characteristics:

1. The compensatory process tends to return the pH back to normal but never completely, except in cases of primary respiratory alkalosis.
2. Compensatory process requires normal functioning kidneys and lungs and take time to occur.
3. The lack of compensation in an appropriate interval defines the presence of a second primary disorder.

4. The compensatory response creates a second laboratory abnormality.
5. The appropriate degree of compensation can be predicted.

a. *Metabolic acidosis*: the expected change in pCO_2 is as follows:

$pCO_2 = [1.5 \times (\text{Serum } HCO_3^-)] + 8 \pm 2$ (Winter Formula) or

pCO_2 = last two digits of the pH

b. *Metabolic alkalosis*: the expected change in pCO_2 is as follows:

$pCO_2 = 40 + 0.6\ (\Delta [HCO_3^-])$ or

$\Delta pCO_2 = 0.6\ (\text{Measured } HCO_3^- - 24)$

c. *Acute respiratory acidosis*: The expected increase in bicarbonate is as follows:

$\Delta [HCO_3^-] = pCO_2/10$

d. *Chronic respiratory acidosis*: The expected increase in bicarbonate level is as follows:

$\Delta [HCO_3^-] = 3.5 \times pCO_2/10$

e. *Acute respiratory alkalosis*: The expected decrease in the HCO_3^- level are:

$\Delta [HCO_3^-] = 2 \times pCO_2/10$

f. *Chronic respiratory alkalosis*: The expected decrease in the HCO_3^- level are:

$\Delta [HCO_3^-] = 5 \times pCO_2/10$

As mentioned earlier, the primary defect in metabolic acidosis is fall in HCO3 which can occur due to one of the following three mechanisms:

a. Excess acid production that overwhelms renal capacity for excretion, e.g. diabetic ketoacidosis.
b. Loss of alkali that leaves unneutralized acid behind, e.g. diarrhea.
c. Renal excretory failure, i.e. normal total acid production in face of poor renal function, e.g. chronic renal failure of any cause.

To differentiate between these causes, it is important to calculate anion gap. The anion gap is shown in the following equation:

Unmeasured anion (UA) + Cl^- + HCO_3^- = Unmeasured cation (UC) + Na^+

UA – UC = Anion gap = $Na^+ - (Cl^- + HCO_3^-) = 12$

If the metabolic acidosis is caused by the addition of Cl– as anion; then it will be designated as normal anion gap acidosis, and if the metabolic acidosis is caused by the addition of anion other than Cl-, then it is designated as high anion gap acidosis.

Delta anion gap (ΔAG): It is the difference between the patient's anion gap and a normal anion gap.

ΔAG = observed AG – upper normal AG

ΔHCO_3 = lower normal HCO_3^- – observed HCO_3^-

In an uncomplicated high anion gap metabolic acidosis, delta anion gap is equal to the delta bicarbonate.

Any significant deviation from this rule implies the existence of a mixed acid-based disorder.

a. When delta anion gap (ΔAG) is greater than delta HCO_3^- ($\Delta HCO3^-$), it indicates mixed high anion gap acidosis and primary metabolic alkalosis.
b. When Δ HCO_3^- is greater than ΔAG, it indicates mixed high anion gap and normal anion gap acidosis, or a mixed high anion gap acidosis and chronic respiratory alkalosis with a compensating hyperchloremic acidosis.

Urine anion gap: In patients with a hyperchloremic metabolic acidosis, one can use urine anion gap to distinguish between renal tubular acidosis (RTA) and acidosis caused by diarrhea. Urine anion gap is calculated as follows:

$$(\text{Urine } Na^+ + \text{urine } K^+) - (\text{Urine } Cl^-)$$

A negative urine anion gap suggests diarrhea as a cause of metabolic acidosis where as positive urine anion gap suggests the presence of RTA with a distal acidification defect.

Approach to a Patient with Acid-Base Disorder

The approach to acid-based derangements should emphasize a search for the cause, rather than immediate attempt to normalize the patient. A full consideration of the careful history such as vomiting, diarrhea, sepsis, diabetes, renal disease, alcohol or other toxin ingestion should be given. A detailed physical examination for evidence of fever, signs of volume depletion, tachypnea or bradypnea, hypo- or hypertension should be carried out. Serum electrolytes such as Na+, K+, Cl– and HCO_3– should be measured in every case. A stepwise, conventional, approach is as follows:

Step I: Determine whether the patient is acidemic (pH <7.36) or an alkalemic (pH >7.44).

In mixed disorders, the pH may be in the normal range, but the bicarbonate level, the pCO2 or the anion gap will be abnormal and signal the presence of an acid-base disturbance.

Step II: Is the primary or overriding disturbance

respiratory or metabolic? In the patients with acidemia, an increase in pCO2 levels indicate primary respiratory acidosis and a decrease in bicarbonate levels indicate metabolic acidosis, where as in patients with alkalemia, a decrease in the level of pCO2 levels indicate primary respiratory alkalosis and an increase in the levels of HCO_3– indicate primary metabolic alkalosis.

Step III: Is there appropriate compensation for the primary disturbance? If a respiratory disturbance is present, is it acute or chronic? Compare measured pH with expected change in pH.

Step IV: If a metabolic acidosis is present, is there an increased anion gap?

Step V: If a metabolic disturbance is present, is the respiratory system compensating adequately?

Step VI: If there is an increase in anion gap, is the delta anion gap equal to delta bicarbonate. If not, there is an additional non-gap acidosis or a metabolic alkalosis.

Step VII: Put it all together—what is the most likely diagnosis?

Case 1

A 22 year old P2L2 with home delivery 4 days ago presents with high grade fever and foul smelling lochia

pH=7.32 pCO_2=22.5 pO_2=92

Na=137 K=4.1 Cl=100

HCO_3=11

Answer 1

pH shows acidemia which is associated with decrease in [HCO_3] and hence metabolic.

Compensation: predicted pCO_2 should be = 1.5 X [HCO_3] + 8 + 2 = 1.5 X [11] + 8 + 2 = (16.5 + 8) + 2 = 24.5 + 2.

Given pCO_2 is 22.5; thus appropriate respiratory compensation is present.

Anion gap (AG) = {Na – (HCO_3 + Cl)} = 137-111 = 26; thus wide AG metabolic acidemia (due to sepsis and lactic acidemia)

Case 2

A 26 year old pregnant lady with acute diarrhea is brought to the ER .

Her BP is 105/65 supine & 75/35 sitting position

pH=7.10 pCO_2=18 pO_2=92

Na=131 K=3.0 Cl=116

HCO_3=5.5

Answer 2

pH and HCO_3 are both decreased - shows evidence of metabolic acidemia.

Compensation: predicted pCO_2 = (1.5 X 5.5 + 8) + 2 = 18.25 + 2; hence appropriate respiratory compensation.

Anion Gap = 131 – (116 + 5.5) = 131 – 121.5 = 9.5. Thus normal AG metabolic acidemia (due to diarrhoea) with appropriate respiratory compensation.

Case 3

A 35 year P4 with preeclampsia with LSCS 2 days ago presents with discomfort in the left leg. Her BP is 90/60 HR=100 RR=28 Temp=99.5° F

pH=7.53 pCO_2=16 pO_2=97

Na=136 K=4.0 Cl=100

HCO_3=14

Answer 3

pH and pCO_2 are changed in opposite direction- show evidence of respiratory alkalemia.

Predicted delta

HCO_3 = 2 X 24/14 = 3.4; or predicted [HCO_3] should be 20.6.

However given [HCO_3] is 14. Therefore metabolic acidosis is also present. AG = 136 – 114 = 22; hence respiratory alkalemia with wide AG metabolic acidosis.

Case 4

A 28 year old lady presents with sudden onset severe left sided pleuritic chest pain upon return from long distance air travel. On physical examination, she was cyanosed with raised JVP and BP of 75/50.

pH=7.42 pCO_2=22 pO_2=48

HCO_3=12.6

What is the interpretation?

Answer 4

Since pH is in the normal range, there has to be a mixed disorder. Respiratory alkalosis (hyperventilation due to pain) PLUS metabolic acidosis (hypotension with poor tissue perfusion) coexist. pO2 is low. Consistent with Type 1 respiratory failure

Key Points

- ABG is a very important point of care investigation which is crucial for the diagnosis and management of the critically ill patient.
- ABG gives information about the oxygenation, ventilation, acid base status and also other important information including lactates, electrolytes, glucose,

hemoglobin

- The blood gases are altered in pregnancy due to the physiological changes and hence should be interpreted accordingly
- The metabolic and respiratory compensations are possible only if the kidney and lung are functioning optimally.

Suggested Reading

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Rationale Use of Antibiotics in Obstetric Critical Care

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Introduction

Physiological adaptations during pregnancy are believed to increase the body's vulnerability to a variety of infections, which can occur during the antenatal period, childbirth, after abortion, or in the postpartum phase, thus necessitating the need for using pertinent antibiotics. Pregnancy is a dynamic state with a plethora of physiological changes, and even the most benign infections can lead to unanticipated sepsis, which is a life-threatening condition characterized by multiple organ failure. Sepsis is the leading cause of maternal mortality and a significant factor in severe maternal morbidity globally, accounting for 11% of maternal deaths and ranking as the third most frequent direct cause of such fatalities.

Prompt medical intervention and treatment for suspected infections are vital, as early action can avert complications and protect the health and well-being of both the mother and the child in the short and long term. Though antibiotics form the backbone of antibacterial therapy, their excessive and often inappropriate administration not only leads to untoward long-term health effects on the mother and her fetus but has also led to the emergence of multidrug resistant organisms. This is significantly more common in settings with limited resources where culture and sensitivity testing is infrequently performed.

Antepartum cases of sepsis most commonly originate from nonpelvic sources, whereas intrapartum and postpartum cases are more likely to have a pelvic origin. In 30% of cases, no identifiable source can be determined.

Recommendations for Antibiotic Use

1. **Confirming diagnosis of infection:** There are no clear guidelines to identify the presence of infection. Infection is diagnosed based on the clinical suspicion with supporting radiologic and microbiologic data and, at times, by the response to therapy.
2. **Early administration of appropriate antimicrobials** is one of the most effective interventions to reduce mortality in patients with sepsis. Delivering antimicrobials to patients with sepsis or septic shock should, therefore, be treated as an emergency. However, the use of empirical antibiotics should be limited to patients with sepsis /septic shock and other specific conditions. As far as possible, cultures should be sent before starting antibiotics.
3. **Before starting antibiotics, consider common pathogens** responsible for the particular situation and choose from an institutional antibiogram. According to Antimicrobial Resistance (AMR) Surveillance Network, Indian Council of Medical Research, 2023
   - Gram-negative isolates have high AMR to 3rd Gen cephalosporins
   - Amikacin showed good susceptibility rates among E. coli & P. aeruginosa (close to 70%)
   - Acinetobacter baumannii showed good susceptibility only to minocycline (>75%) and colistin (>95%).
4. Choose an antibiotic with tissue penetration at the site of infection.
   - If polymyxin antibiotics are required for urinary tract infections, colistin is preferred over Polymyxin B in view of the poor penetration of Polymyxin B in the urinary tract.
   - Macrolides have anti-inflammatory and immunomodulating effects in chronic lung conditions.
   - Antagonism demonstrated in vitro and in vivo between penicillin and erythromycin suggests that β-lactam antibiotics and macrolides should not be administered together unless pneumococcal infection is ruled out.
   - Piperacillin-tazobactam should not be used as a first-line treatment for bloodstream infections caused by ceftriaxone-resistant E. coli or K. pneumonia (MERINO trial)
5. **Daily assess the patient for de**-escalating or stopping antibiotics. Procalcitonin levels in the serum can be used to de-escalate or stop antibiotics. However, it is not recommended for diagnosis of infection.
   - Once cultures are available, switch to Narrower-Spectrum Antibiotics
6. **Stop antibiotics** in case of SIRS without bacterial infection. If infection is ruled out, antibiotics should

be stopped. One dose of empirical antibiotic in critically ill patient being evaluated for etiology will not increase AMR.

7. **Control source and reduce the duration of antibiotics** use. Once source of infection is identified, remove the source and duration of antibiotics.
8. **Consider the pharmacokinetics** and pharmacodynamics of the drug and use the appropriate dosage and schedule. Different antimicrobials have different required plasma targets for optimal outcomes.
   - Aminoglycosides and fluoroquinolones- clinical success depends on higher peak plasma levels in relation to pathogen MIC
   - Vancomycin- higher initial and higher trough plasma concentration is required.
   - Beta lactams- longer duration of plasma concentration above the pathogen MIC required for superior microbiological and clinical cures
   - Fluid resuscitation leads to expanded extracellular volume, so a higher initial loading dose should be given.

Causes for delay in initiating antibiotics in sepsis

- Failure to recognize the existence of sepsis/septic shock
- Delay in initiating antibiotics
  - o Due to culture collection
  - o Delay in carrying out orders
  - o Limited IV access- give bolus IV preparations
- Choosing inappropriate empiric antimicrobials
  - o Lack of appreciation of potential for microbial resistance
  - o Lack of consideration of recent previous antimicrobial use by the patient
  - o Inadequate dose of antimicrobial

Critically ill patients with sepsis are different

These patients have

- ◦ Increased frequency of hepatic and renal dysfunction
- ◦ High prevalence of unrecognized immune dysfunction
- ◦ Predisposition to infection with resistant bacteria
- ◦ Increased volume of distribution

In septic shock, early appropriate antimicrobial dosing is crucial, and failure of antibiotics can cause mortality.

Antimicrobial susceptibility should be kept in mind when choosing antibiotics. Following observations have been published in AMR Surveillance Network, Indian Council of Medical Research, 2023

- o Gram-negative isolates have high AMR to 3rd Gen cephalosporins
- o Amikacin showed good susceptibility rates among E. coli & P. aeruginosa (close to 70%)
- o Acinetobacter baumannii showed good susceptibility only to minocycline (>75%) and colistin (>95%).

To start appropriate empiric broad-spectrum antimicrobials

- Start one or more antimicrobials
- Include antifungal/antiviral when indicated. Do not start antifungal in non neutropenic patients. Risk factors for candida are immunocompromised status (neutropenia, chemotherapy, transplant, diabetes mellitus, chronic liver failure, chronic renal failure), prolonged invasive vascular devices (hemodialysis catheters, central venous catheters), total parenteral nutrition, necrotizing pancreatitis, recent major surgery (particularly abdominal), prolonged administration of broad-spectrum antibiotics, prolonged hospital/ICU admission, recent fungal infection, and multisite colonization.
- Consider the following factors while choosing antimicrobials
  - ◦ local epidemiological factors (susceptibility pattern)
  - ◦ Immune status of patient
  - ◦ Recent infection and antimicrobial use
  - ◦ Nosocomial infections could be due to MRSA or vancomycin resistant Entrococci

Commonly used broad spectrum antimicrobials are:

- ◦ Expended range penicillin/ Beta lactamase inibitors- piperacillin/tazobactam or ticarcillin/clavulanate
- ◦ Carbapenem- Imipenem/cilastatin, meropenem or doripenem
- ◦ 3rd /4th generation cephalosporins
- ◦ Glycopeptide antibiotics- Vancomycin, teicoplanin
- ◦ Oxazolidinone- Linezolid
- ◦ Aminoglycosides
- ◦ Polymyxin- colistin, polymyxin B

Empirical Antibiotics according to the source of sepsis and dosages according to ICMR 2022-Treatment Guidelines for Antimicrobial use in Common Syndromes are given in Table 1 & 2

Table 1: Empirical Antibiotics According to the Source of Sepsis

S.No.	Diagnosis	Causative Organisms	Treatment	Remarks
1.	Puerperal sepsis / Septic abortion / chorioamnionitis	Usually polymicrobial Gram positive: Streptococci (A,B,D), S.aureus Gram negative: E.coli, Enterobacteriaceae (Klebsiella,Enterobacter, Citrobacter), Pseudomonas aeruginosa, Proteus mirabilis, Gardnerella vaginalis, Bacteroides Clostridium perfringens, Anaerobes	First Line : Inj. piperacillin-tazobactam Alternative: Inj. Clindamycin + gentamicin	In case of septic shock, use imipenem/meropenem ± amikacin plus vancomycin to cover MRSA
	Sepsis or septic shock with focus unclear		First Line : Imipenem-Cilastatin +/- Amikacin +/- Vancomycin Teicoplanin +/- doxycycline +/- Colistin or polymyxin B Alternative: Meropenem or Cefoperazone –Sulbactam +/- Amikacin +/- Vancomycin or Teicoplanin Use empiric combination therapy with at least two antibiotics of different antimicrobial classes in patients with septic shock cover MRSA	- If risk factors for candida are present add an echinocandin (Caspofungin or micafungin or anidulafungin) -Triazoles are acceptable in hemodynamically stable, less ill patients who have not had previous triazole exposure and are not known to be colonized with azole-resistant species. -Duration: 7-10 day - Monitor Procalcitonin levels to assist in reducing the length of antimicrobial therapy.
2.	Community Acquired Pneumonia (CAP)	Most common: S. pneumonia, H. influenzae. Others: S. aureus Legionella spp., Klebsiella, Pseudomonas/ Acinetobacter, Varicella zoster, and Pneumocystis jirovecii (in HIV patients).13	First Line : Inj. Ceftriaxone with macrolide/ doxycycline Alternative: Cefotaxime, piperacillin-tazobactam with macrolide In suspected cases of Pseudomonas aeruginosa/other enteric gram negative bacteria use Piperacillin tazobactam/ Cefepime/imipenem In place of Ceftriaxone with macrolide/doxycycline	- Add Oseltamivir in case of an ongoing influenza outbreak - Add vancomycin or teicoplanin if CA MRSA is suspected -In case of hypersensitivity to Beta lactams, use respiratory fluoroquinolones (after excluding TB) - In septic shock, Carbapenems favored over combinations of beta-lactam and beta-lactamase inhibitor.

3.	i) Empiric (Ventilator Associated Pneumonia/ Hospital Acquired Pneumonia) ii) Culture proved VAP/HAP	ii) Most commonly (Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa) iii) MRSA	First Line : Cefoperazone –Sulbactam or Piperacillin-tazobactam Either alone or with Amikacin Alternative: Meropenem Or Imipenem-Cilastatin Plus either Amikacin/ Ceftazidime-Avibactam Plus Aztreonam OR Colistin/ polymyxin B (In settings where carbapenem resistance is >20%) ii) Choose any one according to culture sensitivity from: Piperacillin-Tazobactam/ Cefoperazone –Sulbactam/ Imipenem-Cilastatin/ Meropenem/Colistin Polymyxin B iii) First Line : Inj Linezolid Alternative: Inj. Vancomycin or Inj. Teicoplanin	1. – Can use Levofloxacin (750 mg IV q24h) as an alternative to amikacin as a second line anti-pseudomonal agent. –In case of carbapenem resistant organisms, can give nebulized colistin 2. along with IV colistin 3. If prevalence of MRSA >10-20%, Empirical therapy against MRSA recommended 4. Tigecycline is not routinely advised in the treatment of VAP with CRO 5. iii) Reserve Colistin and Polymyxin B where resistance to all other tested antibiotics is present - In Patients with HAP with CRE in septic shock/at high risk for poor outcome, use combination therapy with 2 antibiotics to which the isolate is susceptible over monotherapy -VAP with septic shock, add empiric coverage for MRSA plus CR GNB along with antipseudomonal beta-lactam.
4.	Acute Pyelo-nephritis	• Enterobacteriaceae - 73.2 % • E. coli - 49.24% • Klebsiella spp -17.44% • Proteus spp - 1.4% • Citrobacter - 1.3% • Enterococcus species - 10.9% • Non-fermenting gram-negative bacilli - 8.2% • Staphylococcus aureus - 0.9%	First Line : Piperacillin – tazobactam/Ertapenem • Alternative: Imipenem/ Meropenem/Amikacin	-Dosage adjustment as per eGFR - Duration : minimum of 7 days, upto 14 days for for complicated UTI -Review IV antibiotics at 48 hours, and switch over to oral antibiotics should be considered. - Routine post-treatment urine cultures are not routinely recommended in asymptomatic patients.

6.	Necrotizing fasciitis	Polymicrobial: S. pyogenes, S.aureus, anaerobes, Gram negative organisms	Piperacillin-tazobactam +Clindamycin	- In cases of exposure to fresh water or salt water suspect Aeromonas or V.vulnificus respectively and give Ciprofoxacin + Doxycycline in place of Piperacillin-tazobactam +Clindamycin - Early surgical debridement -Send blood and intraoperative specimens for bacterial cultures. -Consider use of IVIG for streptococcal NF/TSS - Duration: 14 days, if adequate source control achieved

Table 2: Dosages of Commonly Used Antibiotics

Antibiotics	Dosage in adults
Ceftazidime-avibactam and aztreonam	Ceftazidime-avibactam: 2.5 g IV q8h, infused over 3 hours PLUS aztreonam: 2 g IV q8h, infused over 3 hours
Colistin	9 million units as loading dose and then 4.5 million units q12h
Polymyxin B	15 lacs IU as loading dose and then 7.5 lacs IU q12h.
High dose meropenem	2 g IV q8h, infused over 3 hours
High dose imipenem	1g IV q6h, infused over 2 hours
Tigecycline	200 mg IV x 1 dose, then 100 mg IV q12h
Minocycline	200mg IV q12h
Sulbactam	2g IV q6 - 8h
IV Fosfomycin	4-6g IV q6h
High dose ampicillin-sulbactam (2g of ampicillin and 1 gm of sulbactam)	9g IV q8h over 4 hours
Cefoperazone-sulbactam (1g/1g)	2g IV q8h

Recent developments in selecting antimicrobial therapy

Molecular techniques have improved the ability to identify infectious agents that conventional culture methods might overlook. Commercially available methods such as peptide nucleic acid fluorescent in situ hybridization, matrix-assisted laser desorption-ionization/time-of-flight mass spectrometry, and PCR-based systems can detect pathogens in blood samples prior to the positivity of cultures. PCR testing yields positive results in 11% of patients who are clinically suspected of bacteremia but have negative blood cultures.

Conclusion

Early administration of antibiotics reduces maternal mortality in sepsis and septic shock. Antibiotic should be chosen considering local antimicrobial susceptibility. Pharmacokinetics and pharmacodynamics of the antibiotics should be kept in mind for appropriate dosage and schedule. Antifungal/antiviral drugs should be added when indicated.

Key Points

- In septic shock, antibiotics should be started early
- Preferably culture samples should be taken before starting antibiotics
- Pharmacokinetics and pharmacodynamics of antibiotics should be considered while selecting combination therapy, dosing and dose interval
- Give empirical broad spectrum antibiotics
- Full higher loading dose should be given
- Assess daily for deescalation of antibiotics and narrow spectrum once susceptibility report is available
- Early source control is important

Suggested Reading

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Prescribing Oxygen Therapy

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Introduction

Air containing 21% of oxygen is essential for life. The process of oxygenation requires the absorption of oxygen from the atmosphere, transport through the bloodstream, and sufficient oxygenation of the tissues.

A number of illnesses, such as anemia, heart disease, pneumonia, asthma, shock and chronic obstructive pulmonary disease (COPD), can lead to inadequate oxygenation, necessitating the need of supplemental oxygen.

Assessing Oxygenation Status

1. **Pulse oximetry (SpO_2)** is an effective, noninvasive approach to determine oxygenation level. SpO_2 calculates the amount of oxygen saturation of hemoglobin. The target SpO_2 range is 94–98%. The range for SpO_2 is 88% to 92%, for patients with long-term respiratory disorders like COPD. SpO_2 value may be unreliable if a patient has severe anemia and a low hemoglobin content in their blood. A deceptively low SpO_2 level can also be caused by decreased peripheral circulation.
2. Arterial blood gas (ABG) provides a more accurate assessment of the blood levels of carbon dioxide and oxygen. ABG values are done for individuals in need of immediate medical attention due to deteriorating or unstable respiratory conditions. The results of an ABG test measures levels of bicarbonate, pH, carbon dioxide, and oxygen.

Table 1: ABG - Normal Vlaues (non-pregnant)

Value	Description	Normal Range
pH	Acid-base balance of blood	7.35-7.45
PaO_2	Partial pressure of oxygen	80-100mmHg
$PaCO_2$	Partial pressure of carbon dioxide	35-45 mmHG
HCO_3	Bicarbonate level	22-26mEq/L
SaO_2	Calculated oxygen saturation	95- 100%

Hypoxia - A low amount of tissue oxygenation is known as hypoxia. There are numerous causes of hypoxia such as anemia, cardiac and respiratory disorders. A particular kind of hypoxia known as hypoxemia is characterized by a drop in PaO2 as determined by ABG.

Hypercapnia- A high blood carbon dioxide level is known as hypercapnia. It is determined by the PaCO2 level when it exceeds 45 mmHg. Respiratory acidosis results from a drop in blood pH due to elevated carbon dioxide.

Symptoms and Signs

Symptoms and signs of hypoxia include restlessness, tachycardia, tachypnoea, shortness of breath, use of accessory muscles, flaring of nostrils, orthopnoea, air hunger and cyanosis.

Indication of Oxygen Therapy

Oxygen is indicated for hypoxaemia, not breathlessness. Oxygen saturations of 94-98% should be the goal with supplemental oxygen or 88-92% for those at risk of type 2 respiratory failure.

For a patient who has desaturated, a systematic approach is to be followed for prescribing oxygen.

Prescribing Oxygen Therapy

Since acute hypoxia is a medical emergency, oxygen therapy should be administered urgently. Oxygen therapy can be started without a doctor's prescription, even though oxygen is regarded as a medication that needs to be prescribed.

Oxygen flow rate and the fraction of inspired oxygen (FiO_2) should be included in prescription orders for oxygen therapy. The figure on the oxygen flow meter that ranges from 1 L/minute to 15 L/minute represents the oxygen flow rate. Fio2 is the amount of oxygen that the patient breathes in. The FiO2 for supplemental oxygen therapy ranges from 21% to 100% concentration.

Oxygen is delivered at flow rates measured in L/min. For every increase in 1L/min, the fraction of inspired oxygen (FiO2) increases by 4% (e.g. 1L/min = 24% FiO2, 2L/min = 28% FiO2 etc).

Oxygenation Equipment

1. **Pulse Oximeter** – It is a device for measuring a patient's oxygen saturation level at bedside. In absence of underlying respiratory conditions, the SpO2 levels exceeds 92%.

Fig.1. Pulse Oximeter

2. **Oxygen Flow meter –** Wall mounted oxygen supply outlets are specified to be white in colour while air outlets are standardized to be yellow. The oxygenation device is connected to the oxygen flow meter, which is connected to the white oxygen outlets. A valve on the side of the glass cylinder is used to switch on oxygen and regulate its flow rate. The steel ball inside the cylinder and the glass cylinder's numbered lines are used to determine the flow rate.

Fig. 2 Oxygen Flowmeter

3. **Portable Oxygen Tanks -** When a patient is being transported, portable oxygen tanks are utilized. It can be connected to oxygenation devices for delivering oxygen to the patient. During transport one should be sure that the tank is turned on, has enough oxygen for usage and has the right flow rate adjusted.

Fig 3: Portable Oxygen tanks

Oxygen Delivery Devices

In clinical practice various oxygen delivery devices are used for delivering supplemental oxygen to a patient.

1. Nasal Cannula

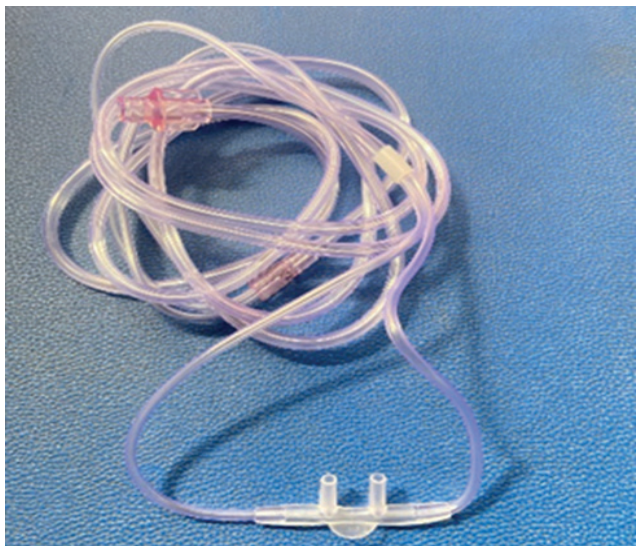


Fig 4: Nasal Cannula

The most basic oxygenation device is a nasal cannula, which has a tubing with two short prongs that are placed into the patient's nostrils. The tube is attached to the oxygen flow meter. For patients receiving oxygen for extended period of time or flow rates higher than 4 L/minute, humidification is required to prevent drying up of the mucosa.

The nasal cannula works well with stable patients who need less oxygen. It is used for both short-term and for long-term oxygen therapy as in COPD patients.

Flow rate: The FiO2 level can range from 24 to 44% when using nasal cannulas, which can have a flow rate of 1 to 5 L/min. This is because FiO_2 increases by 4% for every litre of oxygen.

Benefits: Nasal cannulas are disposable, affordable, and simple to use. The patient can eat and converse while on nasal cannula.

Limitations: The device can become loose while the patient is sleeping. Patients who mouth breathe or have blocked nose, a deviated nasal septum, or nasal polyps are less likely to benefit from nasal cannulas.

2. High-Flow Nasal Cannula

The is an oxygen delivery system that can provide up to 100% humidified oxygen at a flow rate of up to 60L/min. It is used in sick patients and needs close observation.

3. Simple Face Mask

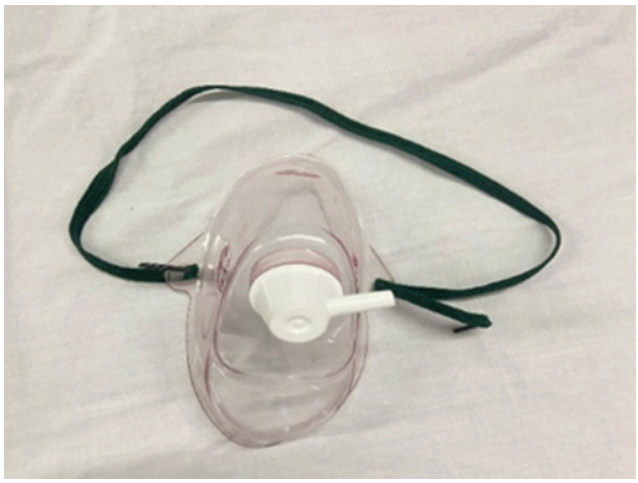


Fig 5: Simple Face Mask

The simple face mask is placed on the patient's mouth and nose to deliver oxygen. The patient exhales carbon dioxide through exhalation ports, on the side of the mask. An elastic band is placed around the back of the head which secures the mask in place. A metal clip near the top can be pressed over the nose for a close fit.

Flow Rate: Oxygen concentration (FiO_2) levels of 35%–50% is achieved by simple masks at a flow rate of 6–10 L/min. If the flow rate is lower than 6 L/min it may cause the patient to rebreathe the expelled carbon dioxide.

Benefits: Moderate oxygen concentrations are provided by face masks. The fitting of the mask determines how effectively oxygen is administered through the simple mask.

Limitations: Face masks must be taken off during meals. It cannot be applied in patients who have claustrophobia.

4. Non-Rebreather Mask

Fig 6. Non-Rebreather Mask

It is a mask which has a reservoir bag that is connected by tubing to a flow meter. The patient breathes in through the reservoir bag during inspiration as it has one-way valve, which also directs carbon dioxide out through the exhalation ports during expiration. The non-rebreather masks are used in patients who are able to breathe on their own but need greater oxygen concentrations to maintain adequate blood oxygenation levels.

Flow rate: A non-rebreather mask is adjusted to provide a flow rate of 10 to 15 L per minute. The non-rebreather mask can provide 60% to 80% FiO_2 when fitted properly.

Benefits: Patients who are able to breathe on their own can receive high oxygen concentrations noninvasively with the non-rebreather masks.

Limitations: Non-rebreather masks have one-way valve, which increases the risk of suffocating in case the gas flow is disrupted. The patient cannot eat or converse while wearing the mask.

5. Partial Rebreather Mask

The partial rebreather mask looks similar to the non-rebreather mask. The partial rebreather has no one-way valve, allowing the patient's exhaled air to mix with the inhaled air. A partial rebreather mask provides 35–50% FiO2 at a flow rate of 10–15 L/min.

6. Venturi Mask

Fig.7 Venturi Mask

Patients with COPD who need extra quantity of oxygen are prescribed venturi masks. The face mask has adaptors that adjust the flow rate to reach FiO_2 between 24% and 60%. The venturi adapter is usually set by respiratory therapists.

Flow rate: The adaptor determines the flow rate. One must consult the respiratory therapist before altering the flow rate.

Benefits: Patients get a particular predetermined quantity of FiO_2.

Venturi masks are colour-coded based on the FiO2 delivered:

Blue = 24% (set at 2L/min)

White = 28% (set at 4L/min)

Orange = 31% (set at 6L/min)

Yellow = 35% (set at 8L/min)

Red = 40% (set at 10L/min)

Green = 60% (set at 15L/min)

Other Modalities for Oxygenation and Ventilation

1. Continuous Positive Airway Pressure Device (CPAP)

Fig 8. CPAP

Patients who require assistance in maintaining an open airway, such as those with obstructive sleep apnoea, should use CPAP devices. A prescription is necessary for a CPAP machine. It consists of a machine that continuously supplies mild air pressure to prevent the patient's airways from collapsing. It is connected to a customized mask that covers the patient's mouth or nose. The adaptor that attaches oxygen using a flowmeter has pre-set settings. It has an attached humidifier. Distilled or sterile water should be used in the humidifier. The mask and tubing should be cleaned periodically in order to prevent infection. The respiratory therapist should set up the FiO2 with the CPAP mask.

2. Bilevel Positive Airway Pressure Device (BiPAP)

Fig. 9 BiPAP

Similar to CPAP devices, BiPAP devices are used to keep airways from collapsing. However, BiPAP devices offer two pressure levels. When inhaling, a certain setting is used, and when exhaling, a lower pressure level is used. The BiPAP devices provide a non-invasive substitute for mechanical ventilation and intubation for patients experiencing acute respiratory distress.

3. Bag Valve Mask (Ambu Bag)

Fig. 10 Ambu Bag with mask

A bag valve mask, also referred to as "Ambu bag," is a portable equipment used for patients who have respiratory arrest or respiratory failure. The gadget differs from other devices as it helps with oxygenation, ventilation, and the flow of air into and out of the lungs. It is important to use the correct size of Ambu bag for the patient. The mask should be sealed to the patient's face. At least two rescuers are required. One squeezes the bag and concentrates on timing and quantity, while the other conducts a jaw thrust manoeuvre, clamps the mask to the patient's face with both hands, and ensures a leak-proof mask seal.

Flow rate: To achieve 100% FiO_2, the flow rate for a bag valve mask connected to an oxygen source should be set to 15 L/minute.

Benefits: Patients having respiratory failure or respiratory arrest can receive urgent aid using a bag valve mask before additional help arrives. It is portable and can be used to hyper oxygenate patients prior to tracheal suctioning and other operations that may result in hypoxia.

Limitations: The compression rate and depth need to be carefully monitored. In case of respiratory failure, the bag compressions must be timed to the patient's inhalations. Overinflating can lead to complications.

4. Endotracheal Intubation and Mechanical Ventilation

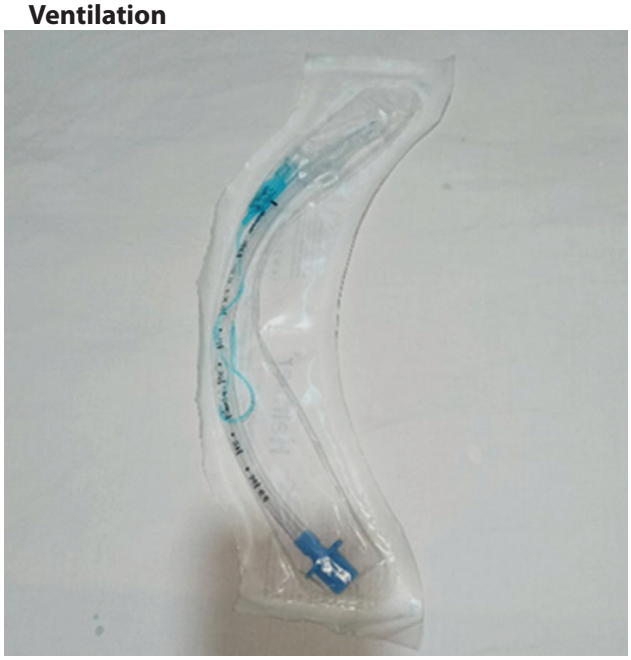


Fig. 11 Endotracheal Tube

The endotracheal tube (ET) maintains a secure airway in patients who have respiratory failure or respiratory arrest. An inflatable cuff is used to seal the ET tube inside the trachea. Mechanical ventilation or a bag valve mask are used to deliver oxygen.

Mechanical Ventilator It is connected to an endotracheal tube to support breathing in patients with respiratory failure or arrest. FiO2 can be set from 21-100%.

Fig.12 Mechanical Ventilator

5. Tracheostomy- Tracheostomy is done as a planned or emergency procedure. It is a surgically created opening that extends from the patient's neck to the trachea. A tracheostomy tube is inserted through the opening into the trachea to keep the airway open and to deliver oxygen.

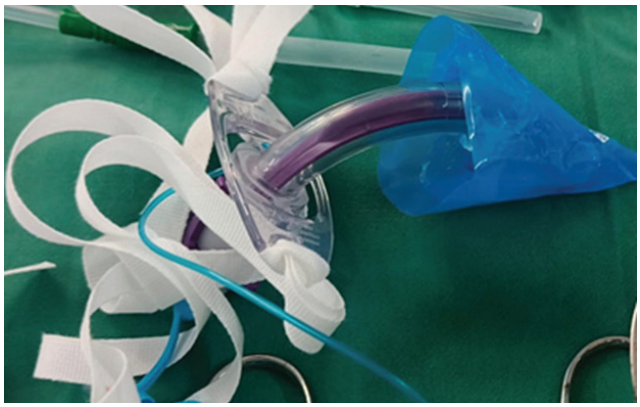


Fig 13: Tracheostomy Tube

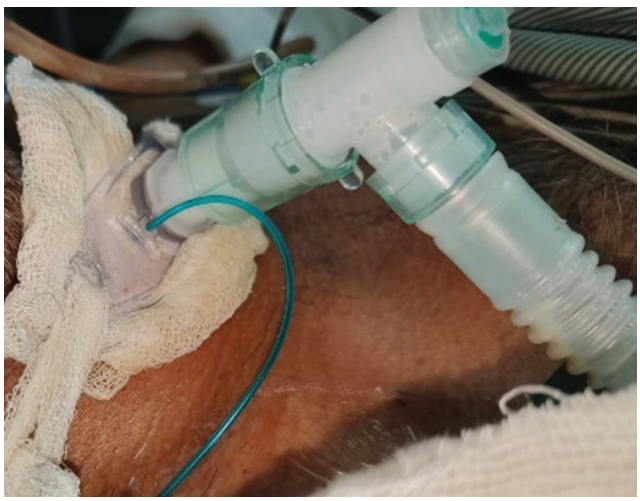


Fig 14: Tracheostomy

Flow Rates and Oxygen Percentages

When administering oxygen to a patient the oxygen flow rates should be set correctly for the type of device used.

Table 2: Flow Rates and Oxygen Percentages for various oxygen delivery devices

Device	Flow Rates and Oxygen Percentage
Nasal Cannula	Flow rate: 1-6L/min FiO2: 24 % to 44%
High-Flow Nasal Cannula	Flow rate: upto 60L/min FiO2: Up to 100%
Simple Mask	Flow rate: 6-10L/min
	FiO2:28% to 50%
Non- Breather Mask	Flow rate: 10 to 15 L/min FiO2: 60-80% Safety note: The reservoir bag should always be partially inflated
CPAP, BiPAP, Venturi Mask, Mechanical Ventilator	Use the settings as provided by respiratory therapist
Bag valve mask	Flow rate: 15 L/min FiO2: 100%

Ref: Oxygen Therapy. -Chapter11: https://www.ncbi.nlm.nih.gov/books/NBK593208/

Oxygen Prescription

Oxygen is a drug and must be prescribed on a drug chart.

Prescription should consist the following specifications:

- Target oxygen saturation
- Oxygen delivery device
- Desired flow rate/FiO2
- Instructions for escalation if a patient's oxygen saturation drops below a certain level should be clearly noted on the prescription

Prescribing Oxygen

If the patient is not breathing start resuscitation and ask for assistance. Airway insertion and high-flow oxygen (15L/min) application via bag-valve-mask ventilation is required.

If the patients is critical but breathing and not at risk of type 2 respiratory failure, high-flow oxygen (15L/min) should be administered with a non-rebreather mask.

Use a Venturi mask to start at a lower FiO_2 and titrate if the patient is in danger of type 2 respiratory failure. Aim for oxygen saturations between 88 and 92%.

Increasing Oxygen Levels

If the oxygen saturations does not reach the target within 3-5 minutes of administering oxygen, the flow rate/FiO_2 (if using a Venturi mask) should be increased.

If the patient becomes critical, increase to 15L/min via a non-rebreather mask

If the patient is not critical, consider increasing oxygen by increments (e.g. from 3L via nasal cannulae to a white Venturi mask – FiO_2 28% at 4L/min)

If a patient's oxygen requirements increase so much that they do not respond to 15L/min via a non-rebreather mask she may need high-flow nasal oxygen (HFNO)/continuous positive airway pressure (CPAP)/non-invasive ventilation (NIV)/intubation and ventilation. This is a complex decision based on various factors, including the patient's ABG results

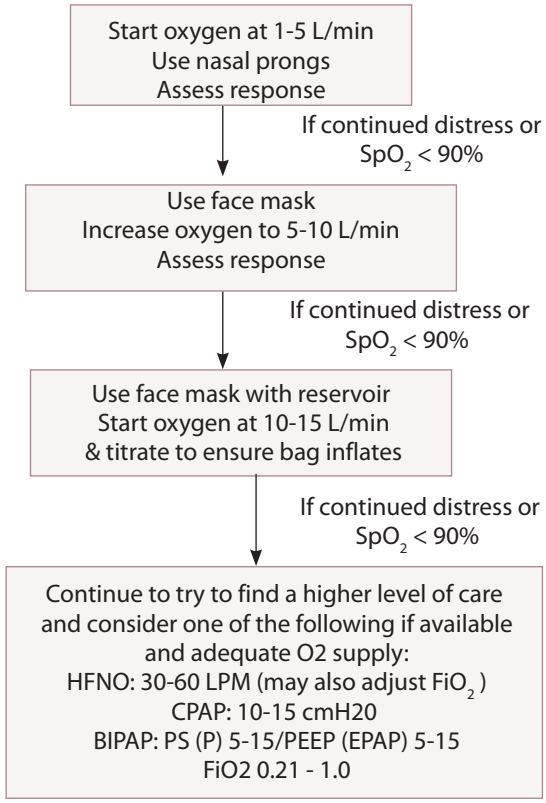
Options for Escalation

High-flow nasal oxygen (HFNO): compared to a non-rebreather mask, can deliver oxygen at a greater FiO_2 (up to 100%) and flow rate (up to 60L/min). It is available in high-dependency/intensive care environments.

Continuous positive airway pressure (CPAP): used in type 1 respiratory failure (PaO_2 <8.0kPa), for example cardiogenic pulmonary oedema

Non-invasive ventilation (NIV): used in type 2 respiratory failure (PaO_2 <8.0kPa AND PaCO2 >6.0kPa), for example a COPD exacerbation.

Adult oxygen therapy escalation algorithm



Ref: Michael Lipnick et.al . Overview of oxygen delivery devices - Intermediate - Open Critical Care Feb2023

In case of ongoing respiratory distress or if SpO 2 is less than 90% on 15L/min clinical care decisions should be based on the characteristics of the patient and local resources.

Monitoring Oxygen Saturation

For monitoring oxygen therapy, follow local protocol. The frequency of monitoring should be adjusted which should include oxygen saturation.

Use the P/F ratio to check if the patient's pO2 responds adequately to the supplemental oxygen.

P/F ratio = PaO_2 on ABG ("P") divided by FiO_2 ("F")

The FiO2 must be expressed as a decimal (e.g. 40% FiO_2 = 0.4).

The normal P/F ratio is 55kPa or 400mmHg (depending on whether PaO_2 is measured in kPa or mmHg).

Weaning and Discontinuing Oxygen

The flow rate/FiO2 is weaned if the patient's oxygen saturations remains at the higher end of their target saturations for 4-6 hours consecutively.

Wean by small increments (e.g. from a yellow Venturi/35% FiO2 to a white Venturi/28% FiO2). Document clear instructions.

Once the patient is stable on 1-2L/min via nasal cannula, oxygen may be stopped.

Monitor the patient's oxygen saturations for 5 minutes without supplemental oxygen. If they remain within their target saturations, measure their oxygen saturations in 1 hour.

Oxygen Toxicity

Some studies have shown that over-oxygenating a patient (aiming for saturations 96-100%) is associated with an increased risk of death in acute illnesses.

Increased reactive oxygen species, leading to cellular damage or death.

Systemic vasoconstriction (including cerebral vasoconstriction), leading to organ hypoperfusion.

False reassurance: respiratory deteriorations may be detected later if a patient is left on high-flow oxygen (as it would require a more significant deterioration to desaturate on high-flow oxygen compared to lower-flow oxygen).

Regularly review a patient's oxygen requirement to ascertain if it can be weaned down.

Safe Oxygen Therapy

Oxygen therapy has numerous advantages, but it also has significant risks. Administering oxygen requires caution and adherence to safety regulations.

Oxygen is a medication and should be administered on prescription. Oxygen cylinders should be stored correctly.

Before transferring a patient, check the oxygen levels.

Keep oxygen cylinders upright, chained, or in the proper holders when not in use. Empty or partially full oxygen tanks should be stored separately from full oxygen tanks.

Use appropriate tank holders when transporting a patient on oxygen. The patient's bed should not be used to hold tanks.

Smoking should not be allowed near any oxygen supply equipment as oxygen is combustible.

Even a tiny electrical spark can cause a large fire. It is dangerous to use a gas stove, or heater near oxygen. When using a nasal cannula, stay away from objects that could spark, such as hair dryers, electrical razors, mechanical toys, and synthetic materials that produce static electricity. Avoid using petroleum-based lubricants near the nasal cannula or on the lips.

Conclusion

In acute medical settings, oxygen delivery is commonly utilized to treat a variety of acute and chronic illnesses, making it an essential part of patient treatment. Healthcare workers must be aware of the devices used for oxygen administration and indications of its use. Although administering oxygen is essential for treating hypoxia, it can also result in complications if not handled appropriately. Infection, hyperoxia, and ventilator-induced lung damage are possible hazards that could have a negative impact on patient outcomes. Optimizing oxygen therapy and guaranteeing patient safety require an understanding of oxygen delivery systems and proper use of these devices.

Key Points

- Oxygen is a drug and should be prescribed on a drug chart. In emergency situations, oxygen may be administered before a formal prescription is obtained
- Aim for oxygen saturation (SpO2) of 94-98% in most patients.
- Prescription Details should include target saturation
- The type of oxygen delivery device should be specified.
- Write the appropriate oxygen flow rate in litres per minute (L/min).
- Specify the duration of oxygen therapy (e.g.,

continuous, intermittent).

- Regularly monitor oxygen saturation using a pulse oximeter and ABG.
- Treat the underlying cause of hypoxemia.

Suggested Reading

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Know Your Critical Drugs- Pressors

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Introduction

Obstetric critical care has significantly reshaped how maternal health is approached and especially in today's world with evolving healthcare challenges. With advances in technology, medical research, and multi-disciplinary teamwork, obstetric critical care has improved the prognosis for both mothers and the newborn. Physiological changes during pregnancy mimics some of the alterations seen in critically ill patients. A good clinical acumen and understanding of pharmacotherapy is therefore necessary for ensuring the best possible outcomes for both the mother and the fetus. This chapter focuses on the emergency lifesaving drugs used in Obstetric critical care. It has been depicted in tabular form for ease of understanding.

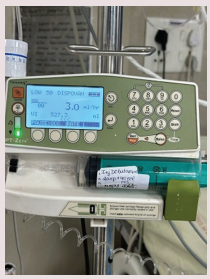
1. Noradrenaline (Norepinephrine)

Category	Details
Generic Name	**Norepinephrine**
Dosage 	- Initial dose: 2–4 mcg/min IV infusion - Titration: Increase by 1–2 mcg/min every 5–15 min based on BP response - Maximum dose: Up to 30 mcg/min (varies based on patient condition) - Administration: Must be diluted in 5% Dextrose or NS and infused via Intravenous access or central line if needed.
Classification	Vasopressor (Alpha & Beta Adrenergic Agonist)
Mechanism of Action	- Alpha-1 agonist: Potent vasoconstriction, increases systemic vascular resistance (SVR) and BP - Beta-1 agonist: Mild increase in cardiac contractility and stroke volume - Minimal beta-2 activity: No significant bronchodilation or skeletal muscle vasodilation
Indications	- Septic shock (first-line vasopressor) - Cardiogenic shock with low systemic vascular resistance (SVR) - Neurogenic shock (e.g., spinal cord injury) - Hypotension post-cardiac arrest
Contraindications	- Hypovolemia (should be corrected with IV fluids before administration) - Peripheral or mesenteric vascular thrombosis (risk of ischemia) - Use cautiously in heart failure (may increase afterload and worsen cardiac function)
Adverse Reactions	- Severe vasoconstriction → Risk of digital ischemia and gangrene - Reflex bradycardia - Arrhythmias (tachycardia or bradycardia depending on vagal tone) - Hypertension (excessive doses) - Extravasation necrosis
Monitoring	- Monitor Blood pressure, Heart Rate, urine output, and capillary refill time - Titrate infusion based on Mean Arterial Pressure (MAP) target (usually >65 mmHg) - Use central venous catheter (prevents extravasation necrosis) - Monitor peripheral perfusion (to prevent ischemia) - Correct hypovolemia before initiation (Fluid resuscitation should be crystalloid based, and if vasopressor is needed, norepinephrine is the first-choice vasopressor)
Storage	- Store at 2-8°C (refrigerated) - Protect from light - Discard if solution turns brown or discolored
Clinical Scenario	- Septic shock patient unresponsive to fluid resuscitation - Neurogenic shock post-trauma with persistent hypotension

2. Vasopressin

Category	Details
Generic Name	Vasopressin
Dosage 	- Septic shock (continuous IV infusion): 0.01–0.04 units/min (fixed dose, not titrated) - Cardiac arrest (ACLS): 20–40 units IV push (single dose) as an alternative to epinephrine - GI variceal bleeding: 0.2–0.4 units/min IV infusion (max 0.8 units/min)
Classification	Antidiuretic Hormone (Non-Adrenergic Vasopressor)
Mechanism of Action	- V1 receptor activation: Potent vasoconstriction, increases systemic vascular resistance (SVR) and BP - V2 receptor activation: Increases water reabsorption in kidneys → Antidiuretic effect, helps in Diabetes Insipidus - Non-adrenergic mechanism: Does not stimulate alpha or beta receptors, making it useful in catecholamine-refractory shock
Indications	- Septic shock (adjunct to norepinephrine for refractory hypotension) - Vasodilatory shock (e.g., post-cardiopulmonary bypass) - Diabetes insipidus (central DI, not nephrogenic) - Gastrointestinal variceal bleeding (reduces portal venous pressure) - Cardiac arrest (ACLS) (alternative to epinephrine)
Contraindications	- Chronic nephritis with nitrogen retention (risk of worsening kidney function) - Coronary artery disease (risk of myocardial ischemia) - Peripheral arterial disease (risk of digital ischemia and gangrene) - Pregnancy (may cause uterine contraction)
Adverse Reactions	- Digital ischemia & gangrene (high doses) - Hypertension & reflex bradycardia - Myocardial ischemia (especially in CAD patients) - Mesenteric ischemia (gut hypoperfusion) - Water retention & hyponatremia (due to V2 activation)
Monitoring	- Monitor BP, HR, urine output, and sodium levels - Assess for signs of ischemia (cold extremities, mottled skin) - Avoid extravasation (use central line) - Do not titrate doses in septic shock (fixed dosing protocol) - Monitor serum sodium levels (risk of dilutional hyponatremia)
Storage	- Store at 2-8°C (refrigerated) - Protect from light - Once diluted, use within 24 hours
Clinical Scenario	- Refractory septic shock despite norepinephrine infusion - Esophageal variceal bleeding in a patient with cirrhosis - ACLS protocol for cardiac arrest (if epinephrine is unavailable)

3. Dobutamine

Category	Details
Generic Name	Dobutamine
Dosage 	- Initial dose: 2–5 mcg/kg/min IV infusion - Titration: Increase by 2–5 mcg/kg/min every 10–15 minutes based on hemodynamic response - Maximum dose: 20 mcg/kg/min (higher doses may increase risk of arrhythmias) - Administration: Continuous IV infusion through a central line
Classification	Inotropic Agent (Selective Beta-1 Adrenergic Agonist)
Mechanism of Action	- Beta-1 agonist → Increases myocardial contractility and stroke volume, improving cardiac output (CO) - Mild Beta-2 agonist → Causes slight vasodilation, reducing systemic vascular resistance (SVR) - Minimal Alpha-1 effect → No significant vasoconstriction or increased Blood pressure
Indications	- Acute decompensated heart failure (ADHF) - Cardiogenic shock with low cardiac output - Post-cardiac surgery low cardiac output syndrome (LCOS) - Septic shock with myocardial depression (adjunct to norepinephrine)

Contraindications	- Hypertrophic obstructive cardiomyopathy (HOCM) (can worsen outflow obstruction) - Severe aortic stenosis (due to increased myocardial oxygen demand) - Uncorrected hypovolemia (should be corrected with fluids first) - Tachyarrhythmias (risk of worsening arrhythmias)
Adverse Reactions	- Tachycardia & arrhythmias (dose-dependent) - Hypotension (due to mild vasodilation) - Increased myocardial oxygen demand → Can worsen ischemia in CAD patients - Eosinophilic myocarditis (rare but reported) - Hypokalemia (prolonged use may lower potassium levels)
Monitoring	- Monitor HR, BP, cardiac output, and ECG continuously - Assess for arrhythmias (especially atrial fibrillation, ventricular ectopy) - Monitor urine output (indicator of improved perfusion) - Titrate carefully to avoid excessive tachycardia - Avoid abrupt discontinuation (wean off gradually to prevent hemodynamic instability)
Storage	- Store at 2-8°C (refrigerated) - Protect from light - Once diluted, use within 24 hours
Clinical Scenario	- Post-MI heart failure with poor ejection fraction and low cardiac output - Septic shock with myocardial dysfunction (low ejection fraction on echo) If patient has low cardiac output in the presence of adequate volume resuscitation, dobutamine is the treatment of choice.

4. Dopamine

Category	Details
Generic Name	Dopamine
Dosage 	- Low dose (renal): 1–5 mcg/kg/min IV - Moderate dose (cardiac): 5–10 mcg/kg/min IV - High dose (vasopressor): >10 mcg/kg/min IV - Titration: Adjust every 10-30 minutes based on BP and cardiac output
Classification	Inotropic Agent & Vasopressor (Dopaminergic & Adrenergic Agonist)
Mechanism of Action	- Low dose: Dopaminergic (D1) → Vasodilation of renal, mesenteric, and coronary arteries (↑ renal perfusion) - Moderate dose: Beta-1 agonist → Increased HR and contractility (↑ cardiac output) - High dose: Alpha-1 agonist → Vasoconstriction, increases SVR and BP
Indications	- Shock (cardiogenic, septic, hypovolemic) - Heart failure (low cardiac output state) - Bradycardia unresponsive to atropine
Contraindications	- Uncorrected tachyarrhythmias - Ventricular arrhythmias - Pheochromocytoma (can trigger hypertensive crisis)
Adverse Reactions	- Tachycardia, arrhythmias - Hypertension - Tissue necrosis if extravasated - Renal ischemia (high doses)
Monitoring	- Monitor HR, BP, urine output - Use central line to avoid extravasation - Titrate dose carefully to avoid excessive vasoconstriction - Monitor for dysrhythmias
Storage	- Store at 15-30°C - Protect from light
Clinical Scenario	- Cardiogenic shock with poor cardiac output.

Occasionally, patient might need 2 or more inotropic support at a point which can be gradually weaned off depending upon the clinical status. Intensivist and cardiology referral must be sought wherever indicated and multidisciplinary approach is needed as it is critical in management of critically ill patients.

Case Vigenette

35 year old P2L2A1 came to Gynae casualty with history of Dilatation and Evacuation 2 days back. Patient had been running high grade fever for 2 days and was referred in view of deteriorating vitals. At time of presentation, her GCS score was E3V3M4. BP-80/40 mmHg, Pulse 130/ min, feeble (Shock index-1.6). Respiratory rate was 24/min, SpO2 was 70 %. Heart sounds were normal and chest was clear on auscultation. Immediate IV access was secured, in view of collapsed veins, central line was secured. Labs were sent and immediately Fluid resuscitation was given with crystalloids till blood and blood products availability. ABG showed metabolic acidosis with compensatory respiratory alkalosis. In view of poor general condition and non maintenance of saturation on NRBM, patient was intubated at FiO2 60 % . Hemogram (Hemanalyser) was suggestive of anemia (Hb 5.6 g %) and leucocytosis with increased neutrophil count. All investigations including Procalcitonin, NT Pro BNP and Cultures were sent. In view of non sustainability of vitals, Noradrenaline was started and titrated to keep MAP > 65 mm Hg. She was shifted to Obstetric HDU after initial stabilization and was started on broad spectrum higher antibiotics. Bicarbonate correction was given. Bedside Ultrasound was normal. Chest Xray had slightly increased bronchovascular markings. Ecg showed sinus tachycardia. Vasopressin had to be added subsequently as MAP was low. Patient gradually improved and was extubated on day 2. Ionotropic support was gradually tapered and stopped thereafter. Counts which were increased initially improved in following days. She was discharged on Day 7 in stable condition.

Conclusion

Combined, coordinated and methodical approach might help achieve the UN target for Sustainable Development Goal (SDG) for MMR at 70 per 1,00,000 live births by 2030.Pregnancy induces a variety of physiological changes that influence the body's response to medications and when this combines with complexities of critical illness, it becomes crucial to carefully consider medication choices and adjustments to ensure safety and efficacy and thereby imrove health outcomes of mother and fetus.

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Use of Blood and Blood Products in Obstetrics

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Introduction

Transfusion of blood and blood components is a common practice in obstetric wards. Moreover, obstetric conditions associated with the need for blood transfusion are associated with considerable morbidity and mortality, if not properly managed. Obstetric haemorrhage continues to be a major cause of maternal mortality in India with 'substandard management' being a contributor in 80% of the cases. High risk pregnancies with an anticipated loss greater than 1000 ml should be strongly advised to deliver in a setting where transfusion support and intensive care facilities are available.

Few recipients can develop transfusion-transmitted infections as well as suffer immunological sequelae such as red cell alloimmunisation; but the major risk associated with blood transfusion is of a patient receiving an 'incorrect blood component. Hence, strict adherence to correct sampling, cross-match and administration procedures is most important way to avoid these complications.

The blood and its components are transfused primarily to enhance oxygen carrying capacity of blood and / or to replace clotting factors which are either lost, consumed or not produced. Immediate and rapid replacement of sufficient and safe blood and its components becomes essential to save the lives of women. The use of blood and its components has become a lifesaving strategy in management of obstetric haemorrhage in general and PPH in particular.

Anemia of pregnancy is defined as haemoglobin concentration <11gm/dl in first trimester and <10.5 gm/dl in 3rd trimester. Early correction of anemia avoids the need of transfusion and maternal mortality. Decision of transfusion should be both clinical & on hematological basis.

WHO classification of anemia

- Mild: 10-10.9 g/dl
- Moderate: 7-9.9 g/dl
- Severe: 4-6.9 g/dl
- Very severe: < 4 g/dl.

Transfusion is almost always indicated when Hb is less than 7 g/dl to reduce the rate of maternal morbidity and mortality. In India the prevalence of anemia is around 65-75%.

The capacity of tolerating the lower concentrations of Hb depends on

- The rate and magnitude of blood loss
- State of tissue perfusion
- Pre-existing cardiopulmonary disease.

Role of blood transfusion in acute haemorrhage is to maintain tissue oxygenation and reversal or prevention of coagulopathy using appropriate blood component. The management of obstetric haemorrhage is more challenging than haemorrhage in non-pregnant patients because of hypervolemia of pregnancy by approximately 50%. Signs of hypovolemia occur relatively late because of physiological changes in pregnancy. The extent of intravascular volume deficit is not reflected by visual estimates of vaginal bleeding.

The appropriate and rational use of blood and its components is essential for ensuring availability for the needy as well as preventing risk of transfusion transmitted diseases and transfusion reactions like allergic reactions, acute immune haemolytic reaction, delayed haemolytic reactions etc.

Different Components of Blood Transfusion

Blood components intended for blood transfusion are routinely collected as anticoagulated whole blood (450 ml). Most of the donated blood is processed into components:

Packed red cells (PRBCs), platelets, and fresh frozen plasma (FFP) or cryoprecipitate. Whole blood is first separated into PRBCs and platelet rich plasma by slow centrifugation. The platelet rich plasma is then centrifuged at high speed to yield one unit of random donor (RD) platelet and one unit of FFP. Cryoprecipitate is produced by thawing FFP to precipitate the plasma proteins, and then separated by centrifugation.

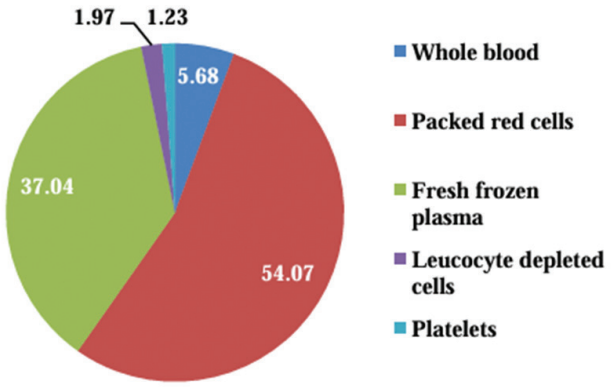

Figure 1: Types of blood and products transfused (Vaid et al, 2020)

Whole Blood: It is stored at 40C to sustain erythrocyte viability. It is the ideal component for the patients who have sustained acute haemorrhage (blood loss >25% of total blood volume) as it improves the oxygen carrying capacity and results in blood volume expansion.

Disadvantages of whole blood are that

- Platelet dysfunction and degradation of some clotting factors occur within 24-48 hours of storage.
- Levels of 2-3 DPG may decrease by 30% in blood stored for greater than two weeks, by 60-70% in three weeks, thus significantly diminishing the ability to release oxygen to tissues.

Packed Red Blood Cells (PRBC): This is prepared by removing 200 cc of plasma from fresh whole blood, to achieve a final hematocrit of 70-80%. They are stored in liquid state at 40 C or frozen at –800 C. It is kept anticoagulated with CPD (citrate, phosphate, dextrose). Survival rate of blood cells decreases from 90% with immediate transfusion to 65% at six weeks of storage. Pre-storage leucocyte reduction of PRBCs is recommended universally to prevent certain adverse reactions i.e. posttransfusion fever, cytomegalovirus (CMV) infections, and alloimmunization. Prestorage filtration appears superior to bedside filtration as smaller amount of cytokine is generated in the stored product.

Cryopreserved RBC: This technique utilizes rapid cooling of PRBC to –800 C in 40% glycerol. 2-3 DPG level remains normal. Antigenic reactions are minimum in this technique. Large quantities of red cells can be stored for many years. But high expense is a significant disadvantage.

Platelets: It is collected by repeated centrifugation of fresh whole blood, and suspension in 30-50 cc of plasma at 220 C. It remains viable for up to five days and is most efficacious if used within 24-48 hours of pooling as they lose ability to produce thromboxane A-2, a potent vasoconstrictor and platelet aggregator gradually over five days. It should be ABO and Rh compatible, since donor plasma is present.

Risk of infectious complications are proportionate to number of donors. Apheresis technology is used for collection of multiple units of platelets from single donor. These single donor apheresis platelets (SDAP) contain the equivalent of at least 6 units of random-donor platelets and have fewer contaminating leukocytes than pooled random-donor platelets. The threshold for the prophylactic platelet transfusion is 10,000/mL. In patients without fever or infections, a threshold of 5000/mL may be sufficient to prevent spontaneous hemorrhage. For invasive procedures 50,000/ ml is the usual target level. Platelets are given either as pools prepared from five to eight random-donor platelets or as a single SDAP. In an unsensitized patient without increased platelet consumption, six to eight units of RD platelets (about 1 unit per 10 Kg body weight) are transfused and each unit is anticipated to increase the platelet count by 5000 to 10000/ mL. Patients receiving multiple transfusions usually get alloimmunized to many HLA and platelet specific antigens and have little or no increase in their post transfusion platelet counts. Patients who may require multiple transfusions are best served by SDAP and leukocyte reduced components to reduce their risk of alloimmunization.

Fresh Frozen Plasma: FFP contains components of the coagulation, fibrinolytic, and complement systems. It is obtained from single donor. It is frozen at 80C, this temperature protects Factor V and VII mainly. It carries the same risk of HIV and Hepatitis as PRBC. It is useful in treating deficiencies in 2, 5, 7, 8, 9, 10, 11, also in Coumarin reversal, antithrombin III deficiency. Type and Rh specific plasma should be used. Urticaria and fatal pulmonary edema can occur. Plasma may also be collected by apheresis. Plasma derivatives such as albumin, intravenous immunoglobulin, antithrombin, and coagulation factors are prepared from pooled plasma from many donors and are treated to eliminate infectious agents.

Alternatives to Transfusion Autotransfusion: It involves collection and immediate reinfusion of patient's own blood for volume replacement and to increase red cell mass. Massive exsanguinations from either blunt or penetrating trauma without gross enteric contamination are best candidates. It eliminates risk of histocompatibility reactions and transfusion transmitted infections. The most common complication is thrombocytopenia.

When patients receive more than 4L of blood, platelet

count may drop to less than 50,000/mL, and risk of acute tubular necrosis increased from debris of plasma-free Hb. There also exist increased risks of air embolism, particulate microemboli, and disseminated intravascular coagulation(DIC).

1. **Pre-Autologous blood storage:** It is similar to PRBC (42 days maximum). Contraindications include significant coronary artery disease, chronic obstructive pulmonary disease, and existence of a hematologic disorder. This is not recommended in pregnancy. Oxygen carrying blood substitutes: i.e. perfluorocarbons and aggregated hemoglobin solutions are presently in various stages of trials.
2. **Intraoperative cell salvage (IOCS)** is the process by which blood shed within the surgical field is retrieved by an anticoagulated suction apparatus and collected within a reservoir from where it is centrifuged, washed and pumped into an infusion bag. This salvaged blood can then be returned to the patient. This process is effective in reducing the need for allogenic red cell transfusion and has been widely used in adult orthopaedic and cardiac surgeries without complications. Cell salvage is recommended for women in whom an intraoperative blood loss of more than 1500 ml is anticipated. The use of IOCS in obstetric practice has been limited, owing to concerns about contamination by amniotic fluid, specifically the risks of amniotic fluid embolism, and by fetal blood cells, particularly the risk of anti-D formation. Common markers of amniotic fluid contamination can be found in the maternal circulation after most deliveries. The IOCS, together with the use of modern leucocyte depletion filters, has been shown to be effective at removing the common markers of amniotic fluid embolism. However, it will not remove fetal blood cells and therefore adequate anti-D immunisation (as determined by Kleihauer test one hour after the procedure) will be required to prevent rhesus immunisation in Rh D-negative women. IOCS has been used during caesarean section in a number of case series and trials without any reported complications related to receiving salvaged blood.

   The National Institute for Health and Clinical Excellence NICE guideline on intraoperative blood cell salvage in obstetrics (IOCS) in obstetrics recommends that, when used, it should be used by healthcare teams who use it regularly and have built up expertise and experience, that patients should consent to its use, and this should be subject to audit and monitoring.

General Principles of Blood Transfusion in Obstetric Patient

- Red cell alloimmunisation is most likely to occur in the last trimester, therefore no pre-transfusion sample should be more than seven days old and ideally should be freshly drawn.
- Only Kell-negative blood should be used for transfusion in women of childbearing age, owing to the high risk of alloimmunisation and subsequent hemolytic disease of the newborn (unless a woman is known to be Kell positive).
- In pregnancy, pre-autologous deposit is not recommended.
- Cell salvage should only be used by healthcare teams who use it regularly and have the necessary expertise and experience.
- If the Hb is less than 7 g/dL in labour or in the immediate postpartum period, the decision to transfuse should be made according to the individual's medical history, age and symptoms.
- If the Hb is less than 7–8 g/dL in postnatal period, where there is no continuing or threat of bleeding, the decision to transfuse should be made on an informed individual basis. In fit, healthy, asymptomatic patients there is little evidence of the benefit of blood transfusion.
- If unexpected severe bleeding is encountered during delivery, investigations should be made postnatally to rule out a bleeding diatheses. These investigations should be performed on a non-urgent basis at least 3–6 months after delivery.

Indications for Transfusion

The various causes of obstetric hemorrhage were divided into early trimester hemorrhage, antepartum hemorrhage (APH) and postpartum hemorrhage (PPH). PPH (35.5%) is the most common indication of blood and blood components transfusion followed by severe anaemia (29.8%) in antepartum and postpartum patients.

This can be attributed to the fact that the hospital is a tertiary care centre where patients with obstetric emergencies are mostly referred from peripheral hospitals.

Anemia can be managed at peripheral hospitals but all cases of PPH with shock are mostly referred to this centre for further management because of unavailability of blood components at peripheral hospitals.

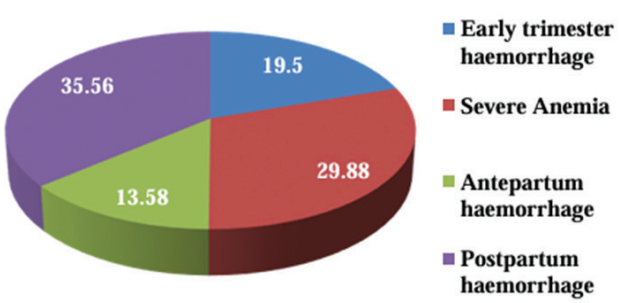

Figure 2: Obstetric indications of blood and components transfusion (Vaid et al, 2020)

Key Points

- Acute blood loss in obstetrics is usually due to placenta praevia, postpartum blood loss and surgery related. This demands early involvement of a consultant obstetrician, anaesthetist, haematologist and the blood bank.
- PCV may be converted to Haemoglobin in gm/dL by dividing it by 0.03.
- One unit of blood lost is compensated by 3 units of electrolytes. A blood loss of 1500 mL is thus compensated by 1500 X 3 = 4500mL Ringer or normal saline infusion.
- In serious hypovolemia, volume therapy with Ringer lactate or normal saline infusion is immediately started. If her circulatory state does not stabilize prompt and permanently as a response to 3000 ml infusion, blood transfusion (or plasma expander) is indicated.
- Once the FFP has been ordered, the blood bank takes at least 30 minutes to thaw and issue the same. During this time, resuscitation should be continued with volume expanding fluids or red cells as appropriate.
- Platelets may be transfused via an unused blood-giving set, although a platelet-giving set reduces wastage because it has less dead space. Transfusion of platelets through a transfusion set previously used for red cells is not recommended.
- Despite the risks associated with transfusions, obstetricians are frequently too aggressive in transfusing blood and blood products to their patients.

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Resuscitation of Pregnant Woman

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Introduction

Maternal mortality signifies the quality of health care services and is hence considered a key factor in predicting resultant materno-fetal outcomes. Cardiac arrest in pregnancy complicates approximately 8.5 in 1,00,000 hospitalizations for delivery with a survival to discharge rate of 59%. Its prevalence in pregnant women varies from 1/20,000 to 1/50,000 and is associated with high neonatal and maternal mortality rates. India contributes to about 1,36,000 maternal deaths out of a total of 5,29,000 maternal deaths occurring globally each year, as per the latest WHO estimates. Cardiopulmonary resuscitation (CPR) in a pregnant female is challenging and requires a multidisciplinary team approach consisting of obstetricians, anesthesiologists, neonatologists, emergency physicians and 'Maternal Blue Code Team' personnel who are well familiar with physiological changes in pregnancy and the resuscitation protocols in a parturient.

Performing CPR becomes tedious in a pregnant patient as the gravid uterus hinders with the process. Hence the caregivers need to have additional knowledge, training, and expertise for CPR in these group of patients. There is need to update oneself regarding the recent guidelines and skill of correct and timely decision making which can help alter the outcomes of resuscitation. The chances of survival post CPR in pregnant women are more as compared to their non-pregnant counterparts (50.6% vs. 28.9%) which is likely due to differences in the two patient populations (such as free existing conditions in non-pregnant population) despite confounding factor adjustments.

Etiology of Cardiac Arrest in Pregnant Women

The causes of cardiac arrest in a pregnant woman can be pregnancy specific or incidental. They are summarized in Table 1. A simple pneumonic ABCDEFGH helps to remember most of them, where A- anaesthesia complications, anaphylaxis, anemia; B- bleeding; C-cardiac causes; D-drugs; E-embolism; F-fever(sepsis); G-general (hypoxia, electrolyte derangements) and H-hypertension.

Table 1- Factors Responsible for Cardiac Arrest in Pregnant Women

S. No	Cardiac Risk factors	Non Cardiac Risk factors	American Heart Association (AHA)
1	Complex congenital heart disease with pulmonary hypertension	Hemorrhage	Bleeding or disseminated intravascular coagulation
2	Valvular disease	Sepsis	Embolism (coronary, pulmonary, and amniotic fluid)
3	Cardiomyopathy	Eclampsia	Anesthetic complications
4	Coronary artery disease	Anemia	Uterine atony
5	Connective tissue disorders	Pulmonary embolism	Cardiac disease (e.g., Myocardial ischaemia, aortic dissection, and cardiomyopathy)
6	Prior cardiac surgery	Complications related to anesthesia	Hypertension (preeclampsia and eclampsia)
7	Triggers such as hemodynamic shifts due to arrhythmias, myocardial ischemia, thrombosis, and electrolyte abnormalities	-	Other (four Hs and Ts from the Advanced Life Support protocol)- H's- hypoxia hypovolemia, hydrogen ions(acidosis),hypothermia or hypo/hyperkalaemia. T's- Tension pneumothorax, Toxins , coronary thrombosis, pulmonary thrombosis, cardiac tamponade.
8	-	-	Placenta abruption/previa
		-	Sepsis

Response to Maternal Cardiac Arrest

The "maternal code blue team or maternal cardiac arrest team" should be activated in the event of a cardiac arrest as this allows for a multidisciplinary team (obstetricians/perinatologists, anaesthesiologists, intensivists, cardiologists, neonatologists and nurses) approach that is required for effective resuscitation via CPR. The guidelines published by American Heart Association in 2015 on CPR in adults and cardiac arrest in pregnancy, changed the initial focus from ABC (Airway, Breathing, Circulation) of CPR to CACDE (Compression, Airway, Circulation, Defibrillation, Extraction) in pregnant women.

High-quality chest compressions with simultaneous aortocaval compression relief, along with attention to the patient's airway and breathing can increase the effectiveness of CPR and hence improve patient outcomes. The various steps in CPR algorithm are described below:-

1. **Manual Left Lateral Uterine Displacement to relieve aortocaval compression-** Even as early as 12 weeks, the inferior vena cava and aorta are compressed by the gravid uterus in supine position but this is particularly evident if the uterine height is at or above the umbilicus. Hence irrespective of the gestational age, manual left lateral uterine displacement (LUD) should be attempted during CPR whenever compression is to be given. It is performed from the left side of the patient by the CPR provider using two hands (Fig. 1). The goal is to pull the uterus leftward and upward towards the ceiling and not downwards (which can further worsen the compression). Manual LUD can also be done from the right side of the patient by pushing the uterus with one hand but effective uterine displacement from the right side is more difficult (Fig. 2). During CPR, a minimal shift of 1.5 to 2 inches is generally needed to optimize stroke volume and venous return. Instead of manually maneuvering the gravid uterus from the abdomen, a wooden wedge or a firm towel roll can also be used for LUD (Fig. 3). As per a trial, manual left LUD produced less hypotension as compared to a 15° lateral tilt in pregnant patients scheduled for caesarean delivery. The effectiveness of chest compressions is compromised with use of wooden wedge or towel (15-30 degrees pelvic tilt) as compared to manual LUD (as the upper torso remains supine in the latter). LUD is also not adequate when soft folded pillows are used. Hence, manual LUD is the recommendation of choice during cardiac arrest in pregnancy especially after 20 weeks, as it not only allows efficient chest compression but also allows other resuscitation maneuvers.

Figure 1- LUD via two hands Figure 2- LUD via one hand Figure 3- LUD via a towel roll

2. Chest Compressions

On the diagnosis of a cardiac arrest, chest

compressions are initiated immediately, even before airway management. Since, no significant vertical cardiac displacement was observed as per MRI in the third trimester of pregnancy as compared to a non-pregnant patient, therefore the placement of hands for CPR is similar for both. They should be placed in the centre of the chest or on the lower third of the sternum overlapped but parallel to each other and compression-ventilation ratio of 30:2 is to be ensured. Patient should be laid supine on a firm surface and chest compressions should be started at the rate of 100-120 per minute (at least 2 inches or 5 to 6 cm deep) allowing for complete chest recovery in between compressions. Interruptions between chest compressions should be minimized to not more than 10 seconds while simultaneous interventions are done.

3. Airway Management and Breathing

The airway patency is checked via head tilt and chin lift maneuver in all cases except where cervical injury is suspected. Initially, a bag and mask is used which is connected to hundred percent oxygen, flowing at the rate of 15 L per minute (administered at the rate of 1 breath every six seconds, or 8-10 breaths per minute). Intubation provides the best opportunity for ventilating pregnant women and decreasing the risk of aspiration due to progesterone induced weakening of lower oesophageal sphincter. Intubation in antenatal women should be performed by an experienced practitioner as it is considered a difficult airway. A smaller endotracheal tube of 6 to 7mm inner diameter should be used for the physiologically edematous and engorged gravid airway. Techniques of video laryngoscopy and supra glottic airway devices insertion may also be used. Cricoid pressure which was primarily preferred to prevent aspiration is not recommended now as a part of standard procedure as it may not necessarily prevent it. Effectiveness of the CPR is indicated by an End-tidal Carbon dioxide levels of greater than 10 mmHg. Double handed ventilation by bag and mask is the ideal method when intubation facility is not available to provide mask seal and sufficient tidal volume for adequate chest rise. Over ventilation can lead to decreased venous return and cardiac output leading to fetal acidosis.

4. Circulation

Pregnancy is a state of physiological haemodilution due to a greater increase in blood volume as compared to blood cell mass. This dilutional anaemia is needed for the normal expected blood loss during delivery. Also the pregnancy is a high metabolic and oxygen requirement state with decreased buffering capacity due to respiratory alkalosis and compensatory metabolic acidosis. Thus two large bore intravenous catheters should be immediately placed using supra-diaphragmatic access at the time of cardiac arrest for adequate resuscitation. Intraosseous placement in the humerus is also an alternative assess route. The ability of medications (given below the diaphragm) from gaining access into the central circulation is compromised due to venous compression and stasis caused by the gravid uterus.

5. Defibrillation

Cardiac rhythm assessment for defibrillation is the next step in CPR algorithm for both pregnant and nonpregnant patients. The electrode pad placement is done on the chest anteriorly and laterally and they are then connected to an external defibrillator which assesses the cardiac rhythm. Energy of 120 to 200 J is required to treat abnormal rhythms like ventricular fibrillation which is same as that required for a non-pregnant patient. The fetal heart rate monitor should be removed prior to administration of defibrillation to prevent fetal electrocution, the basis of this is purely theoretical. In settings where clinicians are least familiar with the rhythm strip, an automated external defibrillator(AED) can also be used.

6. Extraction of the Fetus or the Five Minute Rule for PMCD

Post cardiac arrest even in a non-pregnant patient, the cardiac output is only 30% with high-quality chest compressions[1]. Whereas in case of a parturient CPR effectiveness is even lower which can lead to significantly decrease in blood flow to various maternal vital organs and the fetus. Thus, if return of spontaneous circulation (ROSC) is not established within four minutes (maximum 5minutes), definite resolution of aortocaval compression is needed so preparations are made for expedited delivery of the fetus. This procedure is known as Resuscitative Hysterotomy or PeriMortem Caesarean Delivery (PMCD). It further increases the effectiveness of CPR and materno-fetal survival. When the uterine size is greater than or equal to 20 weeks and ROSC has not been established, the AHA recommends for delivery within five minutes from the time of arrest [5]. If vaginal delivery is imminent, it can also be used, while the others generally require laparotomy. The evidence of correct timing of PMCD from the occurrence of cardiac arrest is derived from various retrospective and prospective studies and reviews. A prospective study conducted in the UK reported a case fatality rate of 42% (28 women died) in 66 cardiac arrest pregnant patients. The ones that died had more likely collapsed at home. PMCD was conducted in 49 women and maternal survival rates of 58% were achieved due

to timely intervention. The study revealed that the time from cardiac arrest to postmortem caesarean delivery was shorter in surviving women ranging from three versus twelve minutes (median interval)[9]. In order to prevent possible delays caused in the patient transfer, the PMCD is to be performed at the location of cardiac arrest itself.

Perimortem Cesarean Delivery Kit and Procedure

The procedure kit includes sutures, needle holders, scalpel blade of ten number, retractors, forceps, towel clips, suction tubes, sponges, uterine packs, Kelly clamps, scissors and neonatal resuscitation equipment. Betadine is poured over the abdomen during the preparation for PMCD at early resuscitation stage by one provider. Incision for PMCD should be made via the method most familiar to the operator. A vertical incision is preferred as it gives an improved access to the upper abdomen and retroperitoneum for aortic compressions and also manual trans diaphragmatic cardiac compressions. After handing over the neonate to the neonatologist the hysterotomy incision is quickly closed (with running locking sutures) at site or in theatre, without hampering the resuscitation process of CPR. The placenta is removed, depending upon the etiology. Due to decreased cardiac perfusion, the surgical field is generally "dry" except in cases where haemorrhage occurred before cardiac arrest.

Assisted instrumental vaginal delivery is preferred when vaginal delivery is nearly imminent and is to be carried out within five minutes following arrest.

7. Intravenous Access and Drugs Used During CPR of Obstetric Patient

Two 14–16-gauge catheters should be used to secure intravenous assess above the level of diaphragm. As described earlier interosseous assess can also be used. Endotracheal tube assess can also be used (in absence of the above two) for double dose of the drugs like epinephrine, lignocaine, diluted in 10 ML normal saline. But the endotracheal route should never be used for certain drugs like calcium gluconate. Table 2, for drugs and their dosages used during CPR in a pregnant woman is given below. The doses for pregnant and non-pregnant patients for almost all drugs used in CPR are similar.

Table 2– Drugs Used in CPR of a Pregnant Women Along with their Doses and Routes of Administration

S. No	Drug Name	Purpose of administration	Dosage
1	Epinephrine (better than vasopressin as the latter causes uterine contractions and decreased uterine blood flow)	Vasopressor	1mg (IV-intravenous /IO-intraosseous) every 3-5 minutes
2	Amiodarone or Lignocaine (Amiodarone favored in pregnancy as local anesthetic toxicity must be kept in mind with lidocaine)	For tiding over pulseless ventricular tachycardia or shock-refractory ventricular fibrillation (non responsive to defibrillation)	Amiodarone -300mg IV/IO with a second dose of 150 mg IV /IO Lidocaine- 1-1.5mg/kg IV/IO for the first dose and 0.5-0.75 mg/kg IV/IO second dose
3	Calcium Chloride or Calcium Gluconate	Magnesium sulphate toxicity Or hyperkalemia	Calcium chloride -10mL of 10% solution IV/IO Calcium gluconate -30mL of 10% solution IV/IO
4	Lipid Rescue	Local anaesthetic toxicity or severe drug toxicity like calcium channel blockers intoxications	20% lipid emulsion IV
5	Sodium Bicarbonate	Severe prolonged metabolic acidosis, tricyclic antidepressant overdose or hyperkalemia	(Not routinely recommended by AHA 2015)

8. Extra Corporeal Cardiopulmonary Resuscitation (ECPR)

ECPR is generally not recommended in pregnancy because of the major challenge of hemostasis due to anticoagulant administration. If ECPR is to be used, the decision is taken timely. This modality is generally used in cases where cardiac arrest etiology is potentially reversible during a small period of mechanical cardiorespiratory support. Conditions that may need ECPR are local anaesthetic toxicity nonresponsive to lipid rescue, pulmonary or amniotic fluid embolism, drug toxicity or acute respiratory distress. There is always a risk of landing in hysterectomy during ECPR to control massive bleeding due to anticoagulants used. A maternal survival of 80% and a fetal survival of 65 to 70% was observed in ECPR usage in pregnant woman.

9. Post-Arrest Care

Post establishment of circulation after resuscitation, the patient monitoring and further management is of prime importance. This has been underrated , as per recent data from American heart association, demonstrating that 73.6% of pregnant patients received ROSC but only 40.7% made it alive upto discharge. Post ROSC patients should be maintained left lateral position for continued aortocaval decompression and should be admitted in ICU for multi-disciplinary patient care and treatment of the baseline cause of cardiac arrest. The post-resuscitation period can be tidal and adequate patient monitoring by experts is required. The key components of management of delivered patients are airway control, circulation maintenance, pain control and prevention of repeat cardiac event (Table 3).

Table 3- Post Arrest Care Components

S.No	Post Resuscitation Care key components	Management
1	Ensuring airway, circulation maintenance	Explained above
2	Prevention of haemodynamic instability and cardiac stunning in post resuscitation period	Vasopressors and inotropes usage to maintain a mean arterial BP of 60 to 65mmHg
3	Prevention of post resuscitation arrythmias	Cardiac pacing and pharmacological therapy
4	Discussion for delivery in undelivered patients	Fetal monitoring till the time patient is undelivered in post ROSC period and discussion for delivery based on gestational age and cardiac arrest etiology
5	Decreasing chances of reperfusion and overall neurological injury in comatose post ROSC patients	Targeted temperature management (TTM) between (32-36 degree Celsius) for at least 24 hours after cardiac arrest as per AHA
6	Glucose control	Maintenance of blood glucose in the range of 140-180 mg/dL
7	Adequate Ventilation	Normal PaCo2 maintenance and an oxygen saturation of 94% or higher (100 percent saturation not needed as it further increases chances of reperfusion injury)

Conclusion

Effective and algorithmic maternal resuscitation leads to increased overall materno-fetal survival. CPR algorithm as per hospital should be strictly followed vertically down by a proper team which is mobile and is available at site. All initial steps of compressions, LUD, ventilation should be simultaneously started (Fig 4). Research related resuscitation maneuvers for relieving aortic compression should be taken in special consideration. The time limit of 5 minutes from cardiac arrest to PMCD may get exceeded and is many times difficult to adhere to, as it depends on multiple factors. These include paucity of on site available resources, variable skill of the providers and other patient associated problems like eclampsia, sepsis, congenital heart disease, hemorrhage and increased maternal age. The healthcare providers need to pay special attention to the resuscitation of obstetric patients especially as more than one live is involved at the same time. The use of newer resuscitation modalities like ECMO is also being promoted. Promotion of institutional deliveries for high-risk mothers, administration of healthcare services as per the obstetric emergency protocol guidelines especially in cases of eclampsia and haemorrhage where massive blood transfusion may be required, provision of resources for on-site PMCD, repeated training of resuscitation team members via seminars, drills and simulation models will overall help in an improved feto-maternal outcome. Proper and detailed knowledge of the national data bases in terms of maternal cardiac arrest causes and various methods of resuscitation and their outcomes is the need of the hour for enhanced patient handling.

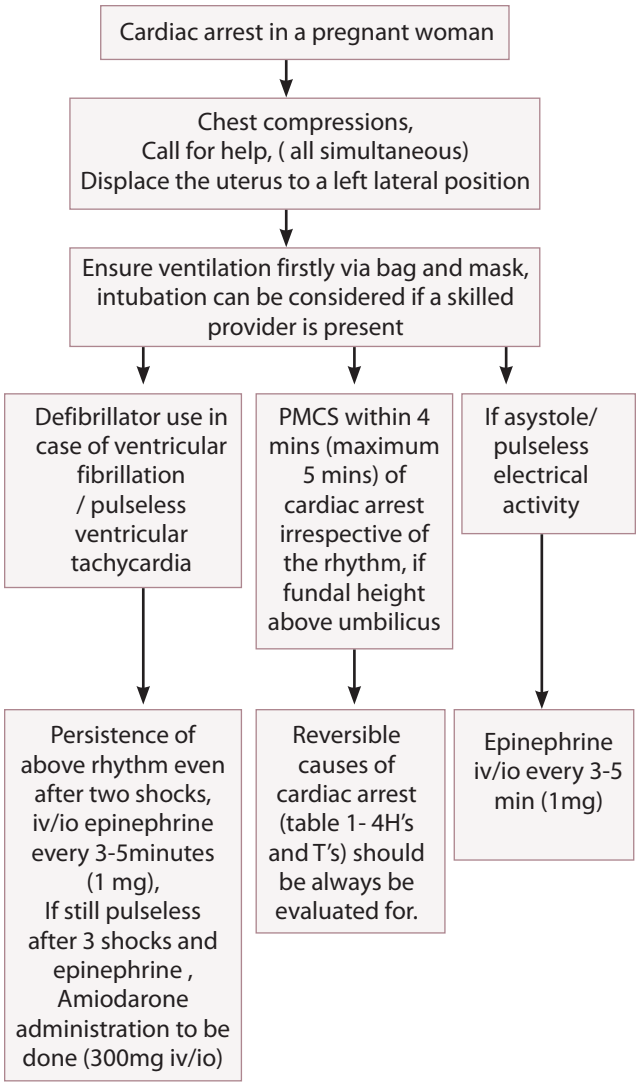

Figure 4- Management Algorithm of Cardiac Arrest in a Pregnant Woman

Key points

1. "Maternal code blue" team should be established in order to provide a multidisciplinary approach during CPR and improve materno-fetal outcome.
2. The team members should be well aware of the physiological changes in pregnancy and the resuscitation algorithms to be used in a parturient.
3. The maternal resuscitation algorithm has been updated from ABC to CACDE by American Heart Association.
4. Relieving aortocaval compression along with high-quality chest compressions and airway maintenance are the preliminary and most important steps of maternal resuscitation.
5. Extraction of the foetus within five minutes of the Cardiac arrest, also known as Perimortem Caesarean Delivery helps improve the overall resuscitation outcome.
6. Timely use of defibrillator is advisable in cases of abnormal rhythms like ventricular fibrillation.

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Mother 'Broughe Dead' - A Clinical, Medicolegal and Ethical Approach for Obstetricians

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Introduction

The term "Mother Brought in Dead" describes an unfortunate and complex situation where a pregnant or postpartum woman is brought to a healthcare facility with no signs of life. Managing such cases requires a systematic, multidisciplinary approach that includes immediate clinical assessment, potential resuscitation, medicolegal documentation, and compassionate communication with the family.

In obstetrics, these cases are particularly challenging because of the dual patient scenario that is the mother and the fetus demanding urgent and well-coordinated action. Furthermore, the legal and ethical implications surrounding maternal deaths necessitate detailed documentation and often an autopsy, especially when the cause of death is unclear or suspicious. This article outlines a structured approach to handling these critical cases efficiently.

Case Scenario

A 32-year-old unbooked pregnant woman (G3P2) at 37 weeks gestation is brought to the emergency department by her husband in an unresponsive state. Her family reports a collapse at home. On arrival, her vital signs are as follows:

- No pulse, no respiration, fixed dilated pupils
- ECG: Asystole
- Blood Pressure: Not recordable
- Fetal heart sounds: Absent
- Physical Exam: Bruising on arms, scratch marks present on neck

Given the sudden and unexplained nature of the maternal death, along with possible signs of physical trauma, an urgent clinical and medicolegal response is warranted, particularly considering the possibility of domestic violence.

Stepwise management of "Mother Brought in Dead"

Step 1: Immediate history from accompanying person, review referral slip, investigations etc., clinical assessment and confirmation of death A structured, evidence-based approach is crucial upon arrival:

- Primary Survey (Airway, Breathing, Circulation):
  - o Assess the patency of airway
  - o Observe for spontaneous breathing (for at least 30 seconds).
  - o Palpate carotid and femoral pulses (minimum 10 seconds).
  - o Examine pupils (fixed, dilated pupils suggest brainstem failure).
- Electrocardiogram (ECG):
  - o Confirm asystole in two leads to declare death.
  - o If pulseless electrical activity (PEA) is noted, investigate reversible causes.
  - o If ventricular fibrillation (VF) is detected, attempt defibrillation.
- Point-of-Care Ultrasound (POCUS):
  - o Assess cardiac activity to confirm the absence of heartbeat.
  - o Check the inferior vena cava (IVC) for trauma-related findings.
  - o Evaluate fetal heart activity (absence confirms intrauterine fetal demise).

Key decision: If death is confirmed, proceed to step 3. If any signs of life are present, continue with step 2 that is resuscitation.

Step 2: Advanced resuscitation (If indicated)

If resuscitation is warranted:

- Follow ACLS protocols: Intubate the patient and secure IV access. Administer epinephrine/ adrenaline every 3–5 minutes.
- Resuscitative hysterotomy: It is considered if the pregnancy is ≥ 24 weeks.
  - o The 4-minute rule: If maternal resuscitation does not show improvement after 4 minutes, initiate a resuscitative hysterotomy.
  - o The 5-minute goal: Uterus must be evacuated within 5 minutes to optimize fetal survival and relieve maternal aortocaval compression.

Step 3: Establishing the cause of death

Determining the cause of death is critical, both for clinical insight and legal accuracy. An autopsy must be advised in all cases of mothers brought in dead for exact cause of death.

Step 4: Medicolegal considerations

All brought dead cases hold legal significance. Obstetricians must adhere to standardized medicolegal protocols, including:

- Mandatory reporting: Any brought in dead mother must be reported to the police and the medicolegal team.
- Thorough documentation: A medicolegal report is prepared. Record the arrival time, clinical findings, ECG confirmation, injuries, interventions, and history given by the family.
- Evidence preservation: If trauma, poisoning, or foul play is suspected preserve clothing and other evidence like urine, blood sample and hand over to the police.
- Death certification: No death certificate is issued by the attending doctor.
- Autopsy: Autopsy is to be advised in all cases for the exact cause of death. If the relatives decline autopsy the same must be recorded in the MLR along with details of the police constable (name, belt no. etc.) informed or present at that time.

Social and Ethical Considerations

- Communication with the family: Deliver the news compassionately, avoiding technical jargon. Explain why an autopsy may be necessary, while considering cultural sensitivities.
- Ethical challenges: Maternal vs. Fetal Survival: Always prioritize maternal resuscitation first.
- Religious/Cultural resistance to autopsy: Address concerns sensitively but adhere to legal requirements.
- Suspicion of domestic violence: It is both an ethical and legal duty to report suspected abuse

Conclusion

Managing "Mother Brought in Dead" cases requires a well-structured, multidisciplinary approach. Obstetricians must be clinically skilled, legally informed, and ethically sound in their approach. This is essential for protecting the attending doctor against medicolegal litigations and for facilitating justice to mother in case of foul play.

Key messages

- Confirm maternal death by clinical assessment, ECG, and ultrasound never assume death on arrival.
- Follow ACLS protocols and consider resuscitative hysterotomy within the "4-minute rule" if the pregnancy is ≥ 24 weeks.
- Detailed documentation and prompt medicolegal reporting are essential.
- Communicate with the family empathetically.

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Management of Brainstem Death in Pregnant Patient

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Introduction

Brain death is defined as the irreversible loss of all functions of the brain, including the brainstem. An evaluation of brain death should be considered in patients who suffered a massive, irreversible brain injury of identifiable cause. A patient determined to be brain dead is legally and clinically dead. The Transplantation of Human Organs Act (THOA) passed by Indian Parliament in 1994 legalised the brainstem death. Maternal brain death raises numerous ethical and legal dilemmas, particularly since it involves two individuals: the mother and the foetus. The complexity of brain death in pregnancy needs a multidisciplinary approach to support both the mother and foetus until successful delivery and, if possible, organ donation after delivery. The critical question is determining the gestational age at which it is appropriate to support the pregnancy. Currently, there is no defined lower gestational age limit that would constrain a physician's efforts to support both the brain-dead mother and the foetus. This article addresses the identification of brainstem death during pregnancy and provides a comprehensive review of recommendations for organ-supportive therapy.

Recognition of Brainstem Death

Steps for diagnosing brainstem death

- Determine a potential cause for underlying brain damage
- Ensure adequate duration of observation before assessing brainstem functions
- Rule out confounding factors that mimic brainstem death
- Perform a comprehensive neurological examination to confirm the brain death
- Conduct ancillary confirmatory tests, if necessary
- Certification of brainstem death
- Offer information and counselling to the family members

Determine a potential cause for underlying brain damage

The diagnosis of brainstem death should never be considered without identifying a clear cause of brain damage. It is important to systematically rule out any confounding factors that could mimic brainstem death. Useful investigations for determining the underlying cause include CT, MRI and cerebrospinal fluid analysis.

Ensure adequate duration of observation

There is no universal agreement on the exact duration of observation needed to confirm that brain function has irreversibly ceased. However, the recommended observation period before evaluating brainstem death is given in the table below.

PATHOLOGY	OBSERVATION PERIOD
Major neurosurgery, aneurysmal bleed	> 4 hours
Traumatic brain injury, spontaneous intracranial bleed	> 6 hours
Hypoxic brain injury from cardiac arrest or drowning	> 24 hours
Suspicion of drug intoxication	> 50-100 hours

Rule out confounding factors that mimic brainstem death

Complicating medical issues such as severe electrolyte imbalances, hypoglycaemia, acid-base disturbances, severe hypothermia (core temperature of ≤ 32°C), significant hypotension (systolic blood pressure < 100 mmHg) and drug intoxication such as alcohol, substance abuse, or recent use of sedatives or muscle relaxants can also present similar symptoms.

Perform a comprehensive neurological examination to confirm the brain death

i. Documentation of coma:

Lack of motor response to a standardized painful stimulus applied along a cranial nerve pathway (pressure on supraorbital groove, temporomandibular joint or trapezius squeeze).

ii. Documentation of the absence of brainstem reflexes:

As brain death progresses, reflexes are lost in a cephalo-caudal sequence. The different tests used to assess the brainstem functions are summarized in the table below.

REFLEX/TEST	CRANIAL NERVES TESTED	LOCATION OF NUCLEI/CENTER
Pupillary light reflex	II, III	Midbrain
Vestibulo-ocular reflex	III, VI, VIII	Midbrain, pons
Oculo-cephalic reflex	III, VI, VIII	Midbrain, pons
Corneal reflex	V, VII	Pons
Pharyngeal gag reflex	IX, X	Medulla
Cough reflex	X	Medulla
Vagus nerve function (atropine challenge)	X	Medulla
Response to painful stimulus along trigeminal nerve distribution	V, VII	Pons
Apnoea test	Respiratory centers	Pons and medulla

iii. Documentation of apnoea:

Apnoea test is carried out only after documenting the absence of brainstem reflexes.[3] During the period of observation, if the patient does not have spontaneous respiration and PaCO2 is 60 mmHg (or 20 mmHg increase over the baseline value), the apnoea test is positive (i.e. supports the clinical diagnosis of brainstem death).

Role of ancillary confirmatory tests in pregnancy

The apnoea test cannot be conducted on a suspected brain-dead pregnant woman due to the risk of hypoxia and hypercarbia, which leads to distress in a viable foetus. As a result, the diagnosis of maternal brainstem death is primarily based on radiological investigations. The recommended ancillary tests are conventional cerebral angiography, electroencephalography, transcranial doppler, cerebral scintigraphy. The time of brain death is usually recorded when the arterial blood gas is reported if apnoea test is performed or when the ancillary testing is completed.

Certification of brainstem death

Institutions should adhere to the protocols established by their respective governments. In India, the THOA outlines the guidelines for declaring brainstem death and comprehensive documentation must be completed on Form 10. This form specifies the procedures for conducting the brainstem evaluation. Two separate examinations, conducted by two distinct medical teams are required to declare brainstem death in adults. The second assessment is typically performed six hours following the first examination.

Offer information and counselling to the family members

When brain death is suspected, the clinician should promptly inform the family and provide maternal somatic support to deliver a viable and healthy infant. It is essential that a senior team member, preferably the primary consultant, counsels the next of kin. Once the clinical criteria for brainstem death have been met, the clinician should formally declare the patient deceased.

Response to Maternal Brainstem Death

After the onset of brain death, it is possible to maintain the somatic functions for an extended period. The pregnant women require specialized medical support and interventions that differ from the support provided to non-pregnant brain-dead patients. The complex physiological alterations associated with pregnancy and brain death, along with the extended duration of hospitalization, pose significant challenges for both the treating medical team and the family. As very few cases of brain-dead pregnant women have been reported in the medical literature, the following is a summary of the available guidelines and recommendations for their management.

Cardiovascular Support

Brainstem injury is initially associated with a sympathetic storm followed by vasoplegia causing significant haemodynamic fluctuations. The minimum monitoring requirements include an arterial line, a central venous catheter and foley's catheterization. Hypertension in this context is rare and typically self-limiting. In cases of prolonged hypertension, short-acting beta blockers like esmolol can be used. Bradycardia should be treated with isoprenaline/adrenaline since atropine is ineffective. Hypovolemia is common and must be promptly

identified and addressed to maintain euvolemia. Initial resuscitation should be done with crystalloids, preferably normal saline or Ringer's lactate. Fluid-resistant hypotension can be managed with vasoactive drugs like vasopressin and dopamine infusion.[4] The goals of resuscitation are summarized as follows:

- Heart rate: 60 – 120 beats/min
- Mean arterial pressure: >70 mmHg
- Systolic blood pressure: >100 mmHg
- Central venous pressure: 6 – 8 mmHg
- Urine output: 1 – 3 ml/kg/h
- Left ventricular ejection fraction: >45%

Respiratory Support

In brainstem death, neurogenic pulmonary edema and ischemia-reperfusion injury contribute to the development of an acute respiratory distress syndrome (ARDS) like condition. In cases of maternal brain death, special attention must be given to mechanical ventilation. To promote the elimination of carbon dioxide from the foetus and due to the effect of progesterone on the respiratory center, the pregnant mother tends to develop physiological respiratory alkalosis. Early tracheostomy should be considered because of the need for prolonged ventilatory support. The lung protective ventilatory strategies include:

- Propped up positioning
- Tidal volume of 6 – 8 ml/kg predicted body weight
- PEEP of 8 – 10 cm H2O
- Frequency adjusted to maintain PaCO2 of 28 – 31 mmHg
- FiO2 titrated to maintain SPO2 > 95%
- Plateau pressure < 30 cm H2O
- Closed circuit tracheal suctioning
- Alveolar recruitment techniques after each disconnection

Endocrine Support

Brain death is associated with the failure of hypothalamo-pituitary-adrenal axis. Hormonal replacement therapy plays a crucial role in correcting haemodynamic instability. The majority of patients develop central diabetes insipidus (DI) due to the failure of posterior pituitary gland. The treatment involves administration of vasopressin, desmopressin nasal puffs and aggressive volume replacement. The recommendation is to initiate levothyroxine in haemodynamically unstable patients, particularly in those with an ejection fraction < 45%. Prednisone or methylprednisolone should be preferred for treating adrenal insufficiency, as they do not readily cross the placenta. Stress-induced peripheral insulin resistance may result in hyperglycaemia, which requires insulin administration.[5]

Temperature and Nutritional Support

Brainstem death is associated with temperature dysregulation leading to hypothermia which can result in intravascular coagulation, decreased myocardial contractility and arrhythmias. The current guidelines recommend maintaining a body temperature above 35°C and continuing feeding as if brain death has not occurred. Total parenteral nutrition should be aimed at supporting a positive nitrogen balance, ensuring maternal weight gain and promoting normal foetal growth.

Infection Control

Pre-transplant donor infection screening and assessment are essential. The primary sources of infection include ventilators, which can cause recurrent pneumonia; urinary catheters, which may lead to UTI; and invasive catheters, which can be a source of septicaemia.[6] These infections are often resistant to antibiotics, making their treatment challenging. Maternal infections should be treated aggressively with the most effective antibiotics.

Haematological Support

Brainstem death triggers the activation of the coagulation system leading to a prothrombotic state with the formation of microthrombi. The risk of developing deep venous thrombosis increases substantially following brain death due to immobility and flaccid paralysis. Current recommendations suggest maintaining an INR < 1.5 and platelets >50,000/mm^3 as therapeutic goals before surgery. Low molecular weight heparin appears to be safe and effective for thromboprophylaxis during pregnancy. Red blood cell transfusions should be withheld unless haemoglobin levels fall below 7 g/dl.

Obstetric and Foetal Considerations

In cases of maternal brain death, it is recommended to screen the maternal serum and to perform foetal ultrasound to ensure there are no congenital malformations or chromosomal abnormalities. Tocolytic therapy may be required to prevent preterm uterine contractions, particularly in the early weeks of gestation. After 24 weeks of gestation, steroids are given for foetal lung maturation and to prevent respiratory distress syndrome. Prolongation of maternal support beyond 32 weeks of gestation is generally unnecessary.

The optimal method of delivery is cesarean section, following which she could be considered as a potential organ donor. The gestational age and the foetal lung maturity are the two most crucial factors influencing foetal outcome.[7] Regular foetal heart rate monitoring using cardiotocography, non-stress testing and serial ultrasound examinations should be conducted to assess intrauterine foetal growth.

Conclusion

The clinical management of brainstem death during pregnancy presents several complex difficulties. When a pregnant woman is diagnosed with brainstem death, a challenging decision arises regarding the continuation of life-sustaining support to preserve foetal viability, if feasible, organ donation following delivery. This decision should involve a multidisciplinary team, including the patient's family and healthcare providers. If somatic support is continued, management should primarily focus on treating complications associated with brain death while ensuring continuous foetal well-being. The objective of extended maternal physiological support is to achieve the delivery of a viable and healthy infant with favourable long-term outcomes.

Key Points

- In India, there is a significant lack of awareness about brain death, its critical role in organ donation and the legal implications surrounding it.
- The diagnosis of brainstem death in a pregnant woman differs primarily due to the impracticality of performing the apnoea test, making the reliance on ancillary confirmatory tests crucial for accurate diagnosis.
- The complex physiological changes resulting from pregnancy and brain death pose considerable clinical challenges, necessitating a multidisciplinary approach for management.
- Establishing an international registry network for brain dead pregnant patients would be beneficial in gathering further insights and experience.

Suggested Reading

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