CRITICAL ILLNESS IN PREGNANCY

INTRODUCTION:

Critical illness in pregnancy increases maternal and fetal morbidity and mortality. The critical illness can be related to pregnancy per se, or can be secondary to a concurrent medical illness. Early identification and appropriate management results in good outcomes with a short ICU stay. Late identification and delayed therapy results in poor maternal & fetal outcomes with development of multiple complications. The altered physiology during pregnancy and lack of familiarity of most practitioners with pregnancy related illnesses is a major hurdle in the pursuit for early identification & definitive management. Moreover a treatment deemed beneficial for the mother may adversely affect the fetus and vice-versa. The overall prevalence of obstetric patients who may require critical care during pregnancy ranges from 1 – 9 in 1000 gestations.1, 2 The maternal mortality due to critical illness is 12 – 20%, but varies significantly between developing and developed countries (440/100000 deliveries in India vs. 12/100000 deliveries in USA).3,4 Hypertensive diseases of pregnancy and obstetric shock remain the leading cause of death in pregnancy.5

A. Physiological changes in pregnancy pertinent to critical care6

Women who gain more than 18 kgs of weight during pregnancy are considered at greater risk for maternal (pre-eclampsia, gestational diabetes) and fetal (increased incidence of operative delivery) complications.7

Cardiac output increases by 30 – 50% at term (6.2 ± 10 Lpm). The increase starts in the first trimester, being secondary to increased stroke volume in first two trimesters, and secondary to an increase in heart rate in the last trimester. It increases by an additional 50% during labor due to expulsion of blood from the uterus during contractions, and an additional 60 – 80% in immediate postpartum period due to auto-transfusion of the uterine blood volume into central circulation along with relief of aortocaval compression. Cardiac output remains elevated for 2 days after delivery gradually returning to normal over a time frame of 2 weeks – 3 months. Blood volume increases by 30 – 50% at term (secondary hyperaldosteronism of pregnancy) and another 300 – 500 ml with each uterine contraction during labor, returning to baseline in postpartum period. RBC mass increases by 15 – 20% (increased serum erythropoietin), which is relatively less compared to the increase in plasma volume resulting in dilutional anemia of pregnancy. Heart rate increases by 15 – 20 bpm at term (83 ± 10 bpm) with an additional increase secondary to pain and stress during labor, returning to baseline in postpartum period. Blood pressure falls by 10 mm Hg till the second trimester thereafter returning to baseline at term, with an additional increase secondary to pain and stress during labor, and again returning to baseline in postpartum period. Systemic vascular resistance reduces during pregnancy (1210 ± 266 dynes cm sec⁻¹), increases during labor, returning to baseline during postpartum period. The central venous pressure and pulmonary artery occlusion pressure remain unchanged as compared to nonpregnant states due to a fall in SVR resulting in accommodation of an increased blood volume in circulation without an increase in pressure. The colloid oncotic pressure reduces (18 ± 1.5 mm Hg) due to a fall in albumin concentration (3.4 gm/100 ml at term) secondary to hemodilution. Oxygen consumption increases by 15 – 20% during pregnancy, with an...
Pulmonary changes include an increase in tidal volume of 40%, an increase in minute ventilation secondary to an increase in tidal volume. The increase in oxygen consumption (VO2) of 30 – 40 ml/min is met by the increase in minute ventilation, simultaneously resulting in a compensated respiratory alkalosis (PaCO2: 30 mmHg = 4 kPa, HCO3: 18 – 21 meq/L, pH 7.40 – 7.47). A “normal” PaCO2 of 40 mmHg in a pregnant lady will be an ominous sign signifying impending ventilatory failure. The reduction in bicarbonate results in pregnant women being more susceptible to metabolic acidosis. Potential changes include increase in left ventricular mass due to hypertrophy and increased water content. The structural remodeling of the heart results in enlargement of the heart chambers, especially the left atrium predisposing to supraventricular arrhythmias. As the uterus enlarges and diaphragm elevates the heart is pushed upwards and to the left resulting in left axis deviation on ECG cardiomegaly on CXR even in the absence of cardiac pathology.

The gravid uterus after 24 weeks produces a significant compression of the inferior vena cava at the level of pelvic brim, in the supine position, reducing the cardiac preload and subsequently the cardiac output by 25 – 30%. Venous return is however maintained by collateral circulation (shunting of IVC blood to the ayzygos system by the intervertebral plexus of veins). A shift to left lateral position, or manual displacement of uterus to left, or left lateral tilt of 25° by placing a wedge below the patient partially alleviates the compression thereby increasing the cardiac output. Despite the reduction in cardiac output, the change in position from lateral to supine is associated with an increase in blood pressure due to an increase in SVR secondary to aortic compression and increased sympathetic outflow. In 5% of patients this position shift however produces marked reduction of venous return resulting in profound reduction in cardiac output producing severe hypotension, bradycardia, hypoperfusion, and occasional cardiovascular collapse. In patients with this supine hypotensive syndrome the cardiac output reduces by an additional 30 – 40%. This hypotension can be exacerbated by neuraxial block of regional anesthesia. Proper positioning of pregnant patient is therefore important in maintaining hemodynamic stability.

Renal changes include an increase in size of kidney by 1.5 cms due to hypertrophy and increased water content. Renal plasma flow increases by 80% & GFR by 25% by 4th week, with GFR increasing to 50% above baseline by 16 weeks of pregnancy. RPF & GFR decrease a little in the third trimester, but return to baseline only 2 months after delivery. Therefore serum creatinine values are lower than normal (0.5 – 0.7 mg/dl) in pregnant women as compared to nonpregnant women. Hence “normal” creatinine values may signify renal insufficiency in pregnancy. BUN values are also reduced in pregnancy. Urinary excretion of protein & glucose is increased in pregnancy. There is a mild dilatation of ureters and pelvic-ureteral system due to effects of progesterone.

Noninvasive hemodynamic monitoring includes the use of impedance cardiography techniques, pulsed wave Doppler ultrasound, and arterial blood pressure measurements to assess systolic and diastolic blood pressures, cardiac output, and stroke volume. These techniques provide noninvasive determinations of central venous pressure and pulmonary capillary wedge pressure, which can be used to guide fluid management in oliguric patients with eclampsia.

B. Issues regarding lab, imaging, and monitoring

Normal lab values during pregnancy:

- Hemoglobin, Hematocrit, Platelet, BUN, Creatinine, Bicarbonate, and Albumin are decreased; WBC, Fibrinogen, and Alkaline phosphate are increased; while AST, ALT, and Bilirubin remain essentially unchanged during pregnancy.
- D-dimers are frequently positive late in pregnancy and so are not useful in diagnosing VTE.
- Fractional excretion of sodium may be misleading if used to guide fluid management in oliguric patients with edemas.

Normal CXR and ECG findings during pregnancy:

The structural remodeling of the heart results in enlargement of all four chambers especially the left atrium predisposing to supraventricular arrhythmias. As the uterus enlarges and diaphragm elevates the heart is pushed upwards and to the left resulting in left axis deviation on ECG cardiomegaly on CXR even in the absence of cardiac pathology.

2D Echo in pregnancy:

Important changes include increase in left ventricular wall thickness, increase in valve annular diameters, mild tricuspid & pulmonary regurgitation (> 90%), and mild mitral regurgitation (33%).

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Critical Illness in Pregnancy
There is a good correlation between Doppler echocardiography and Pulmonary artery catheter (PAC) measurement of stroke volume, cardiac output, ventricular filling pressure, and pulmonary artery pressures.

Invasive hemodynamic monitoring\textsuperscript{16,17}

Studies have demonstrated the benefit of hemodynamic monitoring with the use of PAC in patients of pre-eclampsia/eclampsia with pulmonary edema and oliguric renal failure. Studies also suggest use of PAC in monitoring patients with severe cardiopulmonary disease and refractory septic shock.

CT scan in pregnancy\textsuperscript{18,19}

The potential risks and benefits of CT should be discussed with the patient. An abdominal CT delivers radiation dose of 8.7 – 17.5 mGy while a pelvic CT delivers 2 – 5 rad. The odds for childhood cancer increase after dose of 5 rads. CT contrast is safe and should be administered in the usual manner.

MRI in pregnancy\textsuperscript{20,21}

“Pregnant patients may be approved to undergo MR studies at any stage of pregnancy, so long as the attending radiologist determines the risk-benefit ratio warrants that the study be done” – American college of Radiology guidelines. Written informed consent for MRI during pregnancy is suggested. Gadolinium contrast is not recommended for use in pregnancy.

C. Cardiac arrest in pregnancy\textsuperscript{22}

The frequency of cardiac arrest varies between 1:20000 – 1:30000 pregnancies with survival rates of 6.9%. The major causes of maternal cardiac arrest are trauma, cardiac disease, and embolism. Other causes are unanticipated difficult intubation, complications of pre-eclampsia/eclampsia, sepsis, magnesium toxicity, and anesthetic complications. (BEAU-CHOPS = Bleeding/DIC, Embolism: coronary/pulmonary/amniotic fluid, Anesthetic complications, Uterine atony, Cardiac disease: myocardial infarction/aortic dissection/Cardiomyopathy, Hypertension: pre-eclampsia/eclampsia, Others: standard ACLS differential, Placenta abruption/previa, Sepsis). Cardinal points in preventing cardiac arrest in the critically ill obstetric patient include placing them in left lateral position, giving 100% oxygen, establishing an iv access above the diaphragm, aggressive management of hypotension (SBP < 100 mmHg or < 80% of baseline) and treatment of reversible causes/underlying conditions.

During cardiac arrest the patient is first placed in the supine position and manual left uterine displacement is done. If this is unsuccessful then the patient is placed in a left lateral position tilt of 27 - 30° using appropriate wedge. The quality of chest compressions is compromised in left lateral position. Airway issues include left tilt, weight gain, breast enlargement, edema of airway, difficulty in positioning neck, delayed gastric emptying- predisposing to aspiration, and rapid desaturation. Drugs are administered in standard ACLS doses. Defibrillation is performed at recommended ACLS doses. If internal or external fetal monitors are attached during cardiac arrest it is reasonable to remove them. Management of underlying condition is equally important. PCI is the reperfusion strategy of choice in pregnant patient with ST-elevation myocardial infarction while successful use of fibrinolytics has been reported for massive pulmonary embolism. Cardiopulmonary bypass has been successfully used for life-threatening amniotic fluid embolism. Due care must be exercised in choosing the anesthetic strategy for the pregnant patient as spinal shock can result from regional anesthesia and failed intubation can occur during induction of general anesthe sia.

Perimortem cesarean section (emergency hysterotomy) may improve outcomes in maternal cardiac arrest. The protocol for emergency cesarean section should be activated as soon as cardiac arrest is identified in a pregnant lady with an obviously gravid uterus, i.e. uterus capable of producing significant aortocaval compression (clinically uterine fundus extends above the level of umbilicus). The decision to proceed with a cesarean section should be made within 4 minutes of commencing CPR once immediately reversible causes of cardiac arrest have been ruled out and there is no return of spontaneous circulation. In most cases successful cesarean is followed by immediate return of spontaneous circulation. In cases with an obvious nonsurvivable injury/grave prognosis it is appropriate to move directly for cesarean section. If emergency cesarean cannot be performed in 5 minutes it is advisable to prepare to evacuate the uterus while resuscitation is continued.

D. Epidemiology of critical illness in pregnancy\textsuperscript{4}

In a retrospective analysis of 10 year data (1992 – 2001) pertaining to 928 critically ill obstetric patients from King Edward Memorial Hospital (KEMH) Mumbai being compared to a similar patient population at Houston county hospital, the mean age of Indian patients was 25.4 ± 4.6 years, of which only 26% had received prenatal care (at least 2 prenatal visits) as compared to 86% of Western patients; only 60% of Indian patients presented for admission within 24 hours of onset of illness (vs. 90% for Western patients), with mean APACHE II score of 16 on day 1 (vs. 10 for Western patients); with altered mental status (50%), bleeding (40%), seizures (30%),
fever (27%), dyspnea (23%), and jaundice (21%) being the most common manifestations in this subset (vs. fever – 55%, bleeding – 53%, dyspnea – 44% in Western population).

In both ICUs about 70% of critically ill pregnant patients were admitted with Obstetric disorders. The incidence of Pre-eclampsia/Eclampsia (45%), PPH (15%), Abruptio placenta (6%), Acute fatty liver of pregnancy (4%), APH (4%) in Indian patients was similar to their western counterparts. However the incidence of HELLP syndrome (6% vs. 18%) and puerperal sepsis (7% vs. 15%) was higher in western population. Medical disorders were responsible for only 30% of ICU admissions. Malaria (10%), Viral Hepatitis (6%), Cerebral Venous thrombosis (3.5%), Community acquired pneumonia (3.1%), Aspiration pneumonia (3.1%), Cardiac arrest prior to ICU admission (2.8%) & Rheumatic heart disease (2.1%) were common in Indian patients while Urinary tract infection (10%), Acute abdomen (6%), Aspiration pneumonia (3.5%), Malignancy (3.5%), Asthma, Community acquired pneumonia, & Drug abuse (2.9% each) were common in the western population.

Malaria is more severe in the pregnant women due to change in immune response to Th2 type resulting in loss of acquired immunity against Plasmodium falciparum. Hepatitis E accounts for 60 – 75% of viral hepatitis in obstetric patients, with pregnant ladies being more prone to develop fulminant hepatic failure. In the last few years H1N1 influenza infection has produced severe illness and acute respiratory failure in pregnant women.

E. Organ dysfunction in Obstetric critical illness

The incidence of organ dysfunction in Indian subjects in above mentioned study was reported as follows: Neurological (63%), Hematologic (58%), Renal (50%), Respiratory (46%), Cardiovascular (38%), & Hepatic (36%). DIC was seen in 23% subjects while the maximum MODS score was 5 (3 – 7). In Western subjects Hematological (63%), Respiratory (57%), Hepatic (41%), Renal (37%), Neurological (36%), & Cardiovascular (29%) organ dysfunction were common. Incidence of DIC was 40% with a maximum MODS score of 4 (2 – 6).

The major causes of CNS dysfunction in Indian subjects were Eclampsia, Cerebral Malaria, CNS infections, Hepatic coma, & cerebral venous thrombosis. Important causes of renal failure were Pre-eclampsia, DIC, PPH, hemorrhagic shock, severe Malaria, Leptospirosis, and Acute fatty liver of pregnancy. Hematological failure was predominantly due to Bacterial sepsis and DIC. Respiratory failure was due to Community acquired pneumonia, acute asthma, and ARDS due to abdominal sepsis. Cardiovascular failure was due to Obstetric shock and Rheumatic heart disease. Hepatic dysfunction was predominantly due to acute viral hepatitis in Indian subjects and due to HELLP syndrome in Western subjects.

In the same study organ support (mechanical ventilation, dialysis, component therapy, and Inotrope use) matched the pattern of organ dysfunction in both ICU groups. Obstetric interventions (cesarean section, hysterotomy, hysterectomy, curettage) and induction of labor was significantly more in Western subjects.

F. Outcomes in Obstetric critical care

As highlighted in the above mentioned study the maternal mortality was much higher in Indian patients (25%) as compared to the Western patients (2.7%). Factors leading to adverse outcomes in Indian subjects were lack of antenatal care, delayed presentation, higher severity of illness at presentation, and lack of an aggressive obstetric approach. Organization of health care services and social customs also contributed to low antenatal care and lack of aggressive obstetric approach (non availability of neonatal services)

G. Critical illness due Hypertensive disorders of pregnancy

Hypertensive disorders of pregnancy (chronic hypertension, gestational hypertension, pre-eclampsia, eclampsia, HELLP syndrome – Hemolysis, Elevated Liver enzymes, Low platelets) are the leading cause of maternal mortality and morbidity worldwide. 5% of women with pre-eclampsia/eclampsia require ICU care. These disorders are responsible for 8 – 10% of all preterm births and 50% of women with pre-eclampsia give birth preterm. Hypertension is classified as mild (SBP 140 – 149, DBP 90 – 99), moderate (SBP 150 – 159, DBP 100 – 109), and severe (SBP ≥ 160, DBP ≥ 110).

In chronic hypertension the aim is to keep BP < 150/100 mmHg (no target organ damage) or < 140/90 (in presence of target organ damage). These patients can continue their pre-pregnancy antihypertensive regimen provided it does not contain ACEI, ARB, or Chlorothiazide. There is no need to expedite delivery in these patients if BP is < 160/110 till 37 weeks of pregnancy after which the timing of delivery can be decided upon by the obstetrician. In refractory chronic hypertension delivery must be expedited after steroids for lung maturity (if required) have been given. Postnatal antihypertensive medication should be continued and titrated to BP recordings. If Methyldopa was used it should be dis-
continued on 2nd postnatal day and replaced with another drug.

Patients with severe gestational hypertension (≥ 160/110) require hospital admission and oral Labetalol as first line agent (alternatives – methyldopa & nifedipine) with target SBP < 150 and DBP between 80 – 100 mmHg. Urine should be tested daily for proteinuria, while renal & hepatic function should be monitored on a daily basis. Plan for timing of delivery is same as outlined above for chronic hypertension. Postnatal antihypertensive regimen should be titrated to BP recordings and if BP does not settle down to normal patient referred to a higher center for evaluation.

Patients with pre-eclampsia and all categories of hypertension should be admitted to hospital. Patients with moderate and severe hypertension should be started on oral Labetalol (alternatives – methyldopa & nifedipine) with BP targets < 150 systolic and 80 – 100 mmHg diastolic. There is no need to test urine for proteins after initial assessment while renal & liver function tests and electrolytes should be done three times per week. Delivery should be planned before 34 weeks for patients with refractory severe hypertension. Delivery should be planned after 34 weeks for other patients once their BP has been controlled and corticosteroids for fetal maturit (if required) given. Delivery should be planned within 24 – 48 hours for women with mild – moderate hypertension who have completed 37 weeks. Postnatal BP should be monitored and antihypertensive regimen modified appropriately. If BP does not settle down within 2 weeks the patient should be reviewed at a higher center. Platelet count, creatinine, aminotransferases should be monitored postnatal till within normal range.

Fetal monitoring should include cardiotocography at diagnosis of severe hypertension or pre-eclampsia. If conservative management is planned then ultrasound fetal growth, amniotic fluid volume assessment, and umbilical artery Doppler velocimetry should also be carried out.

During labor BP should be monitored hourly for patients with mild – moderate hypertension and continuously for those with severe hypertension. Patients with severe pre-eclampsia should not be preloaded with IV fluids before establishing low dose epidural analgesia and combined spinal epidural analgesia. Second stage of labor should be limited for women with uncontrolled severe hypertension.

Severe pre-eclampsia is defined by one or more of the following: SBP ≥ 160, DBP ≥ 110, MAP ≥ 120, proteinuria > 5 gm/24 hours, oliguria < 500 ml/24 hours, headaches, visual disturbances, papilloedema, clonus, pulmonary edema, epigastric pain, liver tenderness, AST/ALT > 70 IU/L, HELLP syndrome, and thrombocytopenia (< 100000/mm³). Patients in a critical care setting with severe hypertension, severe pre-eclampsia, who have or have had an eclamptic seizure in should be given iv magnesium sulfate. It should also be considered in patients with severe pre-eclampsia if delivery is planned in < 24 hours. A loading dose of 4 gms in 200 – 250 ml normal saline over 5 minutes is followed by an iv infusion of 1 gm/hour for 24 hours. Recurrent seizures should be treated with a further dose of 2 – 4 gms of magnesium sulfate. Diazepam, Phenytoin, Lytic cocktail should be avoided in patients with eclampsia. Magnesium infusion should be continued for 24 hours after delivery or last convulsion. Magnesium therapy must be monitored for toxicity – respiratory depression, somnolence, loss of patellar reflexes, and infusion rate slowed/stopped in presence of oliguria/rising creatinine level. Therapeutic levels are 4 – 7 meq/L (2 – 4 mmol/L). The antidote for magnesium toxicity is Calcium chloride 1 gm (10 ml of 10% solution) given iv over several minutes. Eclamptic seizures can occur postpartum, usually in first 48 hours, and have been reported up to a period of 23 days. Most patients with eclampsia have neuroimaging done to rule out intracerebral hemorrhage.

The management of severe hypertension according to NICE guidelines involves the use of oral/iv Labetalol (iv bolus 10 – 20 mg every 10 min up to total 80 mg/iv infusion 0.5 – 2 mg/min, watch for fetal bradycardia & neonatal hypoglycemia) or iv Hydralazine (iv bolus 5 – 20 mg every 20 – 60 min). Hydralazine is associated with an increased risk of emergency cesarean section and low Apgar scores. As per the European Society of Cardiology 2011 guidelines a SBP ≥ 170 or DBP ≥ 110 mmHg in a pregnant woman is an emergency and hospitalization is recommended along with treatment with IV Labetalol/oral Nifedipine/oral Methyldopa. Nitroglycerin infusion (5 µg/min increasing at 3 – 5 min up to 100 µg/min) is recommended for pulmonary edema while Nitroprusside infusion (0.25 – 5 µg/kg/min, watch for cyanide & thiocyanate toxicity seen after > 4 hours of infusion) is recommended for a hypertensive crisis. BP should be monitored and therapy titrated accordingly. Target BP is < 150 systolic and diastolic of 80 – 100 mmHg, and one should not aim to normalize blood pressure. 500 ml of IV fluid should be given along with the first dose of hydralazine.

The mode of delivery (vaginal vs. cesarean) is decided upon by clinical circumstances and patient preference. Expediting delivery and aggressive antihypertensive therapy prevent life threatening complications of hypertensive disorders of pregnancy, namely severe hyper-
tension, hypertensive crisis, eclampsia, cerebral hemorrhage, pulmonary edema, acute renal failure, acute hepatic failure, hepatic rupture, and DIC.

**HELLP syndrome** represents a form of severe pre-eclampsia occurring in up to 20% of these patients. Maternal mortality is 1 – 3% while perinatal mortality is 30%. One third of HELLP patients have no evidence of pre-eclampsia. Most cases occur between 27 – 36 weeks while 20% of cases present postpartum usually within 1 – 2 days of delivery. It is characterized by microangiopathic hemolytic anemia (schistocytes on peripheral smear), elevated LDH > 600 U/L, elevated bilirubin 1.2 mg/dl, elevated aminotransferases > 70 IU/L, thrombocytopenia – platelet count < 150000/mm³, which can be sudden and severe. A differential of HUS, TTP, SLE, hepatitis & pancreatitis should be entertained. Treat with Factor VIIa (90 µg/kg, repeated at 20 minutes if there is no response) if all pre-requisites are met. If all measures fail patient is taken up for an urgent hysterectomy.\(^{26}\) Coagulogram should be monitored with ‘point of care’ device - TEG\(^\text{®}\) (thromboelastography – time 1 hour) or ROTEM\(^\text{®}\) (rotational thromboelastometry - time 15 minutes) with use of component therapy & antifibrinolytic being adjusted accordingly.\(^{26}\)

The principles of **damage control resuscitation** should be applied to setting of PPH, and may improve outcome. Aim to achieve normothermia, normal pH, and normal ionized calcium. Keep Hct = 21 - 24%. Administer FFP if APTT > 1.5 times normal, platelets if count < 100000/mm³, fibrinogen if level < 1.5 – 2.0 gm/L. Treat with antifibrinolitics (always if hyperfibrinolysis present). Treat with Factor VIIa if all else fails provided platelets are > 50000/mm³, fibrinogen > 1 gm/L, Hct > 24%, & pH > 7.2.\(^{27}\) Factor VIIa may be potentially beneficial in PPH.\(^{28}\) Coagulogram should be monitored with ‘point of care’ device - TEG\(^\text{®}\) (thromboelastography – time 1 hour) or ROTEM\(^\text{®}\) (rotational thromboelastometry - time 15 minutes) with use of component therapy & antifibrinolytic being adjusted accordingly.\(^{26}\)

I. Acute respiratory failure and ARDS in pregnancy\(^{29}\)

**Critical Illness in Pregnancy**

**Acute respiratory failure and ARDS in pregnancy**

Common causes of acute respiratory failure in pregnancy are Pneumonia, Pulmonary edema, Bronchial asthma, and ARDS. Causes of ARDS in pregnancy can be classified as those **unique to pregnancy** - include Pre-eclampsia, Eclampsia, HELLP, AFLP, Tocolytic associated pulmonary edema, Amniotic fluid embolism, Trophoblastic embolism, chorioamnionitis, & Endometritis; those **modified by pregnancy** - Viral pneumonia including H1N1 Influenza infection, Aspiration of gastric contents, Pyelonephritis, & Malaria; and those **unaffected by pregnancy** - standard causes of ARDS. Little data is available on ARDS in pregnancy and most management strategies have been extrapolated from general ARDS population. Pregnancy related ARDS can occur upto 6 weeks postpartum. ARDS in antenatal period carries a mortality of 23% which increases to 50% in postpartum period.\(^{30}\) Multiple organ dysfunction has been reported as the most common cause of maternal death. ARDS in pregnancy is associated with high rate of fetal death.

Adequate fetal oxygenation requires a PaO2 of ≥ 70 mmHg (SpO2 ≥ 95%) \(^{31}\). Limited data suggest that PaCO2 of 45 – 55 mmHg can be tolerated by high risk neonates \(^{32}\). Clearance of fetal PaCO2 by placenta requires a gradient of 10 mmHg.\(^{33}\) Hence maternal PaCO2 < 45 mmHg which corresponds to pH > 7.3 is a reasonable goal in late pregnancy. A trial of NIV can be given in select patients. The goals of mechanical ventilation are same as promulgated by the ARDS Network trial.\(^{34}\) Though it is expected that pregnant women could tolerate higher plateau pressures due reduced chest wall

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compliance, in pregnant women with ARDS the main contribution to reduced compliance of respiratory system is from lung injury and not due to chest wall. Rescue strategies are similar to those followed for general patients with ARDS. The indications for delivery should be standard obstetric indications in absence of any evidence suggesting improved outcome in setting of ARDS.

Amniotic fluid embolism is a life threatening condition which usually occurs within 24 hours of delivery. It presents with acute hypoxemic respiratory failure, coagulopathy/bleeding, hypotension/shock, right heart failure, & seizures; and this combination of ARDS, shock, and coagulopathy should be considered as Amniotic fluid embolism unless proved otherwise. The reported incidence is between 1:8000 – 1:80000 deliveries with maternal mortality of 85%. The presence of amniotic fluid in the pulmonary circulation is not diagnostic of this syndrome as it can also be seen in normal pregnant women. There is no definitive management. Organ support should be given as required. Fetus should be delivered urgently to prevent fetal loss. Role for Aprotinin and Activated C has been tried for this syndrome with some benefit.

H1N1 Influenza infection has been associated with severe disease and poor outcomes in pregnant women. Although pregnant women represent only 1 – 2% of population, they accounted for 7 – 10% of hospitalized patients, 6 – 9% of ICU admissions, and 6 – 10% of fatalities. The risk of death is markedly increased in the third trimester especially when co-infected with HIV. Fetal morbidity & mortality is also increased due spontaneous abortion, preterm labor & birth, and fetal distress. Treatment with neuraminidase inhibitors Oseltamivir/Zanamivir should be started as soon as possible in pregnant women.

J. Cardiac disease in pregnancy pertaining to critical care

Cardiac diseases are either identified prior to pregnancy or present for the first time during pregnancy. They are a leading cause of maternal mortality ranging from 0.4 – 6% depending upon the cardiac lesion. Pregnant women have a predisposition to develop pulmonary edema due several reasons – increased blood volume, reduced blood viscosity, decreased colloid oncotic pressure, and rapid fluid shifts in the immediate postpartum period. Patients with good cardiac reserve tolerate pregnancy well with most cardiac decompensation occurring in the immediate postpartum period. Patients are also predisposed to develop the supine hypotensive syndrome hence proper positioning is important. Normal signs in pregnancy include distended neck veins, peripheral edema, hyperventilation, loud S1, loud S3, ejection systolic murmurs, & continuous murmurs (venous hum & mammary souffle). ECG may show a left axis deviation along with non-specific ST-T changes. CXR will show enlarged cardiac shadow with prominent lung markings. Hence one must be careful in diagnosing heart disease in pregnancy.

Peripartum risk of various cardiac lesions can be classified as: Highest risk lesion – Pulmonary hypertension > 80 mmHg, Eisenmenger syndrome, NYHA IV, & presence of Cyanosis; high risk lesion – unstable ischemic heart disease, moderate to severe left ventricular obstruction (aortic valve area < 1.5 cm²/mitral valve area < 2 cm²/LVOT gradient > 30 mmHg), Cardiomyopathy with LVEF < 30%, NYHA III, dilated aortic root/Marfan’s/Ehlers-Danlos, moderate pulmonary hypertension, prosthetic heart valve, AICD, h/o TIA/CVA; intermediate risk lesion – stable ischemic heart disease, moderate to severe valvular insufficiency, Cardiomyopathy with LVEF 30 – 50%, NYHA II, mild to moderate pulmonary hypertension, poorly controlled SVT; low risk lesion – ASD, VSD with normal pulmonary pressures, MVP with or without MR, NYHA I, PPI, SVT with good control.

General management involves multidisciplinary team care, 2D Echo in early pregnancy, third trimester, and with change in clinical status, and close monitoring during labor, delivery, and up to 72 hours postpartum. Vaginal delivery is the preferred option for cardiac patients. Patients should be maintained in neutral fluid balance. Early and good anesthesia should be provided – it reduces cardiac work. Regional anesthesia should be given in a way which minimizes hypotension as cardiac lesions may be exquisitely preload dependent. Invasive BP monitoring is preferable for lesions where BP needs continuous monitoring. PAC may be beneficial for complicated cardiovascular lesions.

For rheumatic mitral stenosis if symptoms persist despite optimal medical therapy percutaneous balloon mitral valvuloplasty, commissurotomy, or even valve replacement may be required. Open procedures are associated with higher fetal loss, and although surgery can be performed anytime during pregnancy the risk to fetus is lowest in second trimester. Atrial fibrillation is managed in the same way as for the nonpregnant patient. During labor good regional anesthesia producing excellent pain control along with optimal positioning, fluid balance, pressure control, and limiting second stage of labor are recommended.

Peripartum Cardiomyopathy occurs in 1:3000 – 1:15000 pregnancies. Mortality varies between 9 – 56%
being highest in those with persistent cardiomegaly at 6 months. Causes of death include end stage heart failure, arrhythmias, and thromboembolism. Management is as standard for acute decompensated heart failure except that ACEI are not used in pregnancy, they are started after delivery. During pregnancy afterload reduction can be achieved with calcium channel blocker/hydralazine. Refractory failure may require intra-aortic balloon counterpulsation (IABP) and extracorporeal membrane oxygenation (ECMO). Early experience with Bromocriptine has been promising but large RCTs are awaited. Prolactin, especially its 16-kDa angiostatic and proapoptotic form has been implicated in the pathogenesis of Peripartum Cardiomyopathy. Bromocriptine use has been shown to improve left ventricular ejection fraction, and the composite endpoint of death, NYHA class III/IV, and LV ejection fraction < 35% at 6 months in a small single center pilot study. Acute myocardial infarction can occur anytime during pregnancy – antepartum: 38%, intrapartum: 21%, postpartum (< 6 weeks): 41%. Maternal mortality ranges from 7 – 35% with maximum mortality in antenatal cases.39,40 CK-MB is mildly elevated in pregnancy so troponins are more specific for diagnosis. Coronary angiography, angioplasty, stenting, can be carried out safely during pregnancy.41 PCI is preferable if facilities are available as fibrinolytic use is a relative contraindication during pregnancy.

Cardiac arrhythmias are managed in the same way as for nonpregnant patients except that Amiodarone should not be considered as a first line agent for stable arrhythmias due to its effect on fetal thyroid. Defibrillation & Cardioversion are done in the usual manner. Anticoagulation is done using heparins with low molecular weight heparins being the preferred agent.

Tocolytic induced pulmonary edema is a complication of β-mimetic tocolysis with an incidence of 0.15%.42 Aetiology is multifactorial. Treatment involves immediate discontinuation of offending drug and standard management of pulmonary edema.

K. Venous thromboembolism in pregnancy

Pregnant women are five times more prone to develop VTE than nonpregnant women and it remains a leading cause of maternal death.43,44 Diagnostic valuation remains unchanged except that D-dimers become positive late in pregnancy hence are not useful in this scenario. Compression ultrasonography (CUS) of proximal veins is the initial screening test for DVT. If equivocal Magnetic Resonance Venography (MRV) can be used for confirmation as it does not carry the radiation risk of contrast venography. V/Q scanning carries a low radiation risk for the fetus but is recommended for diagnosis of PE. If V/Q scan is indeterminate and there is no evidence of DVT it is followed by conventional angiography using a brachial approach. This carries a lower risk of radiation than spiral CT.

Low molecular weight heparins (LMWH) are the anticoagulants of choice for DVT prophylaxis.45 Elastic compression stockings can also be used for DVT prophylaxis. Role of IVC filter has not been studied in this setting. Fibrinolytic therapy is recommended for patients presenting with massive PE, in this setting the benefits outweigh the risks of intracerebral hemorrhage.

L. Hepatic issues in pregnancy pertaining to critical care47

The liver may become more difficult to palpate due to the enlarging uterus while telangiectasia & palmar erythema may be seen in up to 60% of normal pregnancies due to the hyperestrogenic state. Mild elevation of aminotransferases may be seen in pre-eclampsia/ eclampsia, HELLP syndrome, drug induced liver disease, Hyperemesis Gravidarum, Budd Chiari syndrome, acute fatty Liver of pregnancy, & hepatic rupture. Marked elevation of aminotransferases is seen in toxemia with liver infarction, Budd Chiari syndrome with portal vein thrombosis, acute hepatic rupture, shock, & drug induced liver disease.

Acute fatty liver of pregnancy (AFLP) occurs in the third trimester usually between 34 – 37 weeks and carries 18% maternal & 23% fetal mortality. Initial symptoms may be non-specific and it is important to distinguish this disease from HELLP syndrome and pre-eclampsia (Table 1). Salient features include hypertension, jaundice, thrombocytopenia, coagulopathy, elevated aminotransferases, and hypoglycemia. Maternal morbidity is due to coagulopathies (especially DIC), hepatic encephalopathy, fulminant hepatic failure (rapidly developing FHF), pulmonary edema, and renal failure. Early delivery is recommended while treatment is supportive. The syndrome usually resolves within 2 – 3 days postpartum.48

The differential of fulminant hepatic failure in pregnancy includes AFLP, which may or may not be associated with pre-eclampsia, disorders which are part of pre-eclampsia – HELLP syndrome, hepatic hemorrhage, rupture, and hepatic infarction, infections – Hepatitis E and Herpes Simplex virus hepatitis. The mortality rate for pregnant women with Hepatitis E is 20%. Serology helps to identify these viral infections as cause of hepatic decompensation.

M. Acute Renal Failure in pregnancy49

BUN and creatinine values are lower than normal in
pregnant women. In a study from Mumbai the incidence of Acute Renal failure (using SOFA score) was 35% in critically ill pregnant ladies admitted to an ICU of a tertiary care center. In most cases the renal failure was part of a Multiorgan failure.50 Medical disorders causing ARF include sepsis, malaria, leptospirosis, poisoning, snake bite, pyelonephritis, SLE, renal calculi, drugs, and contrast. Obstetric disorders include pre-eclampsia (incidence - 50%), eclampsia, obstetric hemorrhage, HELLP syndrome (incidence - 62%), AFLP (incidence - 82%), DIC, and postpartum HUS/TTP.51 Causes of ARF in first half of pregnancy include septic abortion, ectopic pregnancy, and medical causes; in second half of pregnancy include pre-eclampsia, medical causes; while causes in postpartum period include hemorrhage, pre-eclampsia, sepsis, HUS, and medical causes; in second half of pregnancy include pre-eclampsia, ectopic pregnancy, medical causes; in second half of pregnancy include pre-eclampsia, medical causes; while causes in postpartum period include hemorrhage, pre-eclampsia, sepsis, HUS, and medical causes.52 7 – 20% of obstetric patients have ARF due to acute cortical necrosis as a result of severe ischemia secondary to shock and DIC. It presents with oliguria and has poor outcome with long term residual renal dysfunction/dialysis dependency for life.

Identification and treatment of underlying cause is foremost. Delivery of fetus may improve maternal and fetal outcomes in eclampsia, HELLP syndrome, and AFLP. Standard principles for prevention and management of ARF apply in pregnancy. The dose of dialysis in acute renal failure in pregnancy is not clear.5,6 The prognosis of obstetric patients with ARF is better as compared to nonpregnant patients. Mortality is 10 – 20% when ARF is part of single organ failure and 30 – 60% when part of MOF.

N. Neurologic issues in Obstetric critical care

Neurologic involvement is seen in > 50% of critically ill obstetric patients. It can be due to preexisting neurological disorders or due to medical disorders which have more severe manifestations during pregnancy e.g. Falciparum malaria, Hepatitis E virus infection, Cerebral venous thrombosis. Altered consciousness is the most common neurological manifestation in these patients. Women with GCS score of ≤ 8 have an increased risk of death (OR 4.7). Important causes of altered conscious-

### Table 1: Differentiating between AFLP, HELLP, and Pre-eclampsia

<table>
<thead>
<tr>
<th></th>
<th>AFLP</th>
<th>HELLP</th>
<th>Eclampsia/Pre-Eclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>↑</td>
<td>Normal, mild ↑</td>
<td>Normal, mild ↑</td>
</tr>
<tr>
<td>ALT</td>
<td>300 IU/L</td>
<td>150 IU/L</td>
<td>60 IU/L</td>
</tr>
<tr>
<td>Ammonia</td>
<td>↑</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Glucose</td>
<td>↓</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>DIC</td>
<td>75%</td>
<td>20 – 40%</td>
<td>Rare</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>↓</td>
<td>Normal or ↑</td>
<td>Normal or ↑</td>
</tr>
</tbody>
</table>

O. Sepsis in pregnancy

The reported rate of bacteremia in pregnancy is 7.5/1000 admissions while the rate of sepsis in this population is 8 – 10%. Most bacteremic patients do not develop sepsis.57-60 The rate of septic shock is also low varying from nil to a maximum of 12% in various studies.57,64 Sepsis is one of the five leading causes of pregnancy related deaths with maternal mortality ratio of > 1000/100000 live births in African countries and < 20/100000 live births in European countries.62 The mortality from septic shock is also low varying between 0 – 3% in most reports, as compared to nonpregnant patients, this is attributed to young age, lack of co-morbid conditions, and a focused site of infection (pelvis). No scoring system has been validated in critically ill pregnant population with studies suggesting that APACHE II score overestimates/underestimates mortality.63-66

Infections predisposing to sepsis are pyelonephritis, chorioamnionitis, septic abortion, and pneumonia. Microbiological agents implicated are aerobic gram negative rods (E. coli), followed by gram positive bacteria (Enterococci, beta-hemolytic streptococcus), mixed (anaerobes – peptostreptococcus, bacteroides), or fungal infections.58,67 Sepsis exaggerates the low SVR state of pregnancy producing profound hypotension and tachycardia. Sepsis induced myocardial dysfunction can produce a profound cardiovascular collapse as increased cardiac output is responsible for maintaining blood pressure in pregnancy. The manifestations of late septic shock in pregnancy therefore include a cold clammy skin (reflex peripheral vasoconstriction), bradycardia, & cyanosis. Sepsis is managed as per the Surviving Sepsis Campaign guidelines. The antibiotic chosen must be safe for the fetus. There is no evidence to suggest harm by Norepinephrine use during pregnancy. There are no data on vasopressin use in pregnancy. The use of Drotrecogin alfa has not been studied during pregnancy with anecdotal reports claiming safety and efficacy. It has been assigned Pregnancy Category ‘C’ by FDA and
Critical Illness in Pregnancy

routine use is not recommended in pregnancy. It may be used if benefits outweigh the risks.

WHAT SHOULD WE DO IN THE INDIAN SCENARIO?
We must identify physicians and establishments in different zones/regions which deal with critically ill obstetric patients. The availability of a standard Intensive Care Unit manned by a qualified Intensivist is a boon. The Obstetric critically ill patient should be dealt with aggressively and one must remember that there are two lives involved. We can also encourage practitioners to acquire experience in the subject of Maternal-fetal medicine as available in some western countries. On a larger scale we must encourage pregnant ladies to report for regular antenatal care and educate them to report early at times of illness. I have reviewed contemporary relevant aspects of Critical illness in pregnancy as it is not possible to review the entire spectrum of obstetric critical illness.

REFERENCES