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Critical Illness in Pregnancy

Part I: An Approach to a Pregnant Patient in the ICU and Common Obstetric Disorders

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Managing critically ill obstetric patients in the ICU is a challenge because of their altered physiology, different normal ranges for laboratory and clinical parameters in pregnancy, and potentially harmful effects of drugs and interventions on the fetus. About 200 to 700 women per 100,000 deliveries require ICU admission. A systematic five-step approach is recommended to enhance maternal and fetal outcomes: (1) differentiate between medical and obstetric disorders with similar manifestations, (2) identify and treat organ dysfunction, (3) assess maternal and fetal risk from continuing pregnancy and decide if delivery/termination of pregnancy will improve outcome, (4) choose an appropriate mode of delivery if necessary, and (5) optimize organ functions for safe delivery. A multidisciplinary team including the intensivist, obstetrician, maternal-fetal medicine specialist, anesthesiologist, neonatologist, nursing specialist, and transfusion medicine expert is key to optimize outcomes. Severe preeclampsia and its complications, HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome, and amniotic fluid embolism, which cause significant organ failure, are reviewed. Obstetric conditions that were not so common in the past are increasingly seen in the ICU. Thrombotic thrombocytopenic purpura of pregnancy is being diagnosed more frequently. Massive hemorrhage from adherent placenta is increasing because of the large number of pregnant women with scars from previous cesarean section. With more complex fetal surgical interventions being performed for congenital disorders, maternal complications are increasing. Ovarian hyperstimulation syndrome is also becoming common because of treatment of infertility with assisted reproduction techniques. Part II will deal with common medical disorders and their management in critically ill pregnant women. CHEST 2015; 148(4):1093-1104

ABBREVIATIONS: AFE = amniotic fluid embolism; DIC = disseminated intravascular coagulation; HELLP = hemolysis, elevated liver enzymes, and low platelets; HUS = hemolytic uremic syndrome; LDH = lactate dehydrogenase; MMR = maternal mortality rate; OHSS = ovarian hyperstimulation syndrome; TTP = thrombotic thrombocytopenic purpura

Obstetric patients form a small but important population that may need intensive care. ICU physicians need to be familiar with the unique differences in management when treating two patients simultaneously (mother and fetus). Medical disorders

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present differently during pregnancy. Normal ranges for vital signs and laboratory tests may differ. Potentially harmful fetal effects of x-rays can limit diagnostic options. Moreover, physiologic targets like arterial pressure, Pao_2, and $Paco_2$ may have to be modified to ensure fetal well-being.

Obstetric patients include women admitted during pregnancy or the first 42 days (6 weeks) after termination of pregnancy.[1-3] Although ICU admission rates are comparable in developed and developing countries (200-700 women per 100,000 deliveries),[3-8] maternal mortality differs greatly. In 1990, the maternal mortality ratio (MMR) (MMR = maternal deaths per 100,000 deliveries) was 26 in developed nations and 430 in the developing nations.[9] Over the last 24 years, with improvements in public health systems, better access to health care, and possibly improved intensive care, MMR has declined to 16 (38% decrease) in developed countries and 230 (46% decrease) in developing countries in 2013,[9] but it is still short of the Millennium Development Goal of the World Health Organization, which targeted a 75% reduction in MMR between 1990 and 2015.[9] In this two-part series on critical illness in pregnancy, we review important concepts that are essential for a critical care physician to optimally manage an obstetric patient in the ICU.

Physiology of Pregnancy

Maternal cardiovascular changes start in the first trimester, peak at the end of the second trimester, and then plateau until delivery. Cardiac output increases by 30% to 50% from 8 to 28 weeks' gestation and can worsen underlying cardiac conditions such as mitral stenosis.[10] After the first trimester, supine positioning may decrease cardiac output and cause symptomatic hypotension due to decreased venous return from aortocaval compression. Therefore, pregnant patients in a supine position (on an operating room table or ICU bed) should be tilted 15° to 20° degrees to either side by using a pelvic tilt wedge, to displace the uterus laterally.[11]

Plasma volume increases dramatically and is 50% higher by term. Red cell mass increases less, resulting in "physiologic anemia."[10,12,13] One putative benefit of this is that decreased blood viscosity prevents excessive thromboembolic events by compensating for the hypercoagulable state resulting from an increase in coagulation factors.[13] Another potential benefit is the ability to tolerate 500- to 1,000-mL blood loss during delivery without significant consequence. Patients with preeclampsia have significant intravascular hypovolemia and are more susceptible to the hemodynamic effects of obstetric hemorrhage. In addition, hemoconcentration in preeclampsia increases the risk of placental and other thromboembolic events. Arterial BP initially decreases, reaching its nadir at 28 weeks, gradually increasing to normal at term.[10,13]

Progesterone-mediated increase in tidal volume results in increased minute volume, decreased $Paco_2$, and respiratory alkalosis. Elevation of the diaphragm by the gravid uterus and hormonally induced changes in the shape of the chest wall reduce functional residual capacity, residual volume, and expiratory reserve volume.[13] Glomerular filtration rate increases by 50%, resulting in a low serum creatinine (< 0.8 mg/dL). Renal insufficiency in pregnancy is defined by a serum creatinine of > 1 mg/dL, and renally excreted drugs should be dosed accordingly.[10,13] Delayed gastric emptying and a relaxed esophageal sphincter increase the risk of aspiration during endotracheal intubation, seizures, and altered mental status. Adaptive alteration of the helper T cell immune response in pregnancy to T helper 2 type occurs to facilitate "immune tolerance" of the fetus; this could, however, increase risk of some infections in pregnancy.[14]

During labor, cardiac output increases by 15% to 20% because of autotransfusion of 300 to 500 mL during each uterine contraction; blood volume increases by 500 mL after delivery of the placenta.[10] Neuraxial anesthesia with resultant sympathetic blockade may partially attenuate these changes. Cardiac output is also affected by anxiety, pain, maternal (supine) position, and Valsalva maneuver.[10,13] The leukocyte count may increase to 15,000/μL and, rarely, as high as 25,000/μL. Gastric emptying is further delayed during labor.[10] Diaphragmatic fatigue may sometimes occur following straining during prolonged labor.

Causes of Critical Illness in Pregnancy

Obstetric patients require ICU admission for organ dysfunction caused by obstetric or medical disorders or both (Table 1).[1,2,15] In obstetric literature, these disorders are classified as direct causes of maternal morbidity or mortality if they result from obstetric complications (obstetric hemorrhage, hypertensive disorders of pregnancy, amniotic fluid embolism, fatty liver of pregnancy, and surgical or anesthetic complications of cesarean section). Indirect causes include medical disorders not directly attributable to the pregnant state.[9] Obstetric disorders are responsible for 50% to 75% of ICU admissions, with preeclampsia-eclampsia, obstetric hemorrhage, and pelvic sepsis accounting for 80% of obstetric ICU admissions across all geographic regions

TABLE 1] Conditions That Could Lead to ICU Admission in Pregnancy and the Postpartum Period

Conditions Unique to Pregnancy	Increased Susceptibility During Pregnancy	Unrelated to Pregnancy	Preexisting Diseases That May Worsen
Obstetric hemorrhage	Renal	Diabetic ketoacidosis	Cardiovascular
Placental abruption	Acute renal failure	Cytomegalovirus	Valvular disease
Placenta previa	Infections	HIV infection	Eisenmenger syndrome
Retained placenta (accreta)	Urinary tract infection	Toxoplasmosis	Coarctation of aorta
Pregnancy-induced hypertension	Listeriosis	Community-acquired pneumonia	Cyanotic congenital heart disease
HELLP syndrome	Viral hepatitis E	Drug abuse	Primary pulmonary hypertension
Acute fatty liver of pregnancy	*Plasmodium falciparum* malaria	Trauma	Respiratory
Chorioamnionitis	Coccidioidomycosis		Cystic fibrosis
Amniotic fluid embolism	Varicella pneumonia		Lung transplant
Puerperal sepsis	A(H1N1) infection		Bronchial asthma
Pelvic septic thrombophlebitis	Hematologic		Obstructive sleep apnea
Peripartum cardiomyopathy	Disseminated intravascular coagulation		Renal
Ovarian hyperstimulation syndrome	Venous thrombosis		Glomerulonephritis
Fetal mirror syndrome	Postpartum HUS/TTP		Chronic renal insufficiency
Tocolytic-induced pulmonary edema	Endocrine		Endocrine
Gestational diabetes	Sheehan syndrome		Prolactinoma
Gestational hyperthyroidism	Neurologic		Diabetes mellitus
	Intracranial hemorrhage		Hepatic
	Respiratory		Cirrhosis
	Pulmonary thromboembolism		Hematologic
	Aspiration		Sickle cell disease
	ARDS		Anemia
			Rheumatologic
			Scleroderma
			Polymyositis
			Systemic lupus erythematosus
			Neurologic
			Epilepsy
			Intracranial tumors
			Myasthenia gravis
			Multiple sclerosis

A(H1N1) = 2009 influenza A(H1N1); HELLP = hemolysis, elevated liver enzymes, and low platelets; HUS = hemolytic uremic syndrome; TTP = thrombotic thrombocytopenic purpura. (Adapted with permission from Soubra and Guntupalli.[2])

(Table 2).[1,4,5,7] In contrast, medical disorders show wide geographic variation. Bronchial asthma, community-acquired pneumonia, complex urinary tract infections, pulmonary thromboembolism, collagen vascular disorders, trauma, and drug abuse are common in developed countries, whereas viral hepatitis, miliary TB, parasitic infections, rheumatic heart disease, and suicidal poisoning are common in tropical countries.[6,8,15,16] Approximately 12% to 45% of ICU admissions are during the antepartum period, 50% are during labor or the first 24 h after delivery, and 10% to 15% are later in the postpartum period.[1,5]

TABLE 2] Indications for ICU Admission in Obstetric Patients in Large Studies From Different Parts of the World

Geographic Region	Worldwide[a]	Range From Various Studies[b]
Patients studied, No.	7,887	174-2,927
Obstetric disorders	73	68-79
Hemorrhage	23.3	17-29
Hypertensive disorders	36.2	26-45
Pelvic sepsis	4.9	7-27
Abortion-related	NA	0.9-12
HELLP syndrome/acute fatty liver of pregnancy	NA	4-19
Medical disorders	27	21-32
Community acquired infection/sepsis	NA	13-21
Bronchial asthma	NA	1.9-3.6
Cerebral venous thrombosis	NA	1.8-3.5
Pulmonary thromboembolism	NA	1.6-3.7
Suicidal attempt	NA	0-1.5

Data presented as % unless otherwise noted. NA = data not available. See Table 1 legend for expansion of other abbreviation.
[a]Data from a systematic review of 40 studies.[3]
[b]Data from large observational studies from North America, Europe, Asia, Africa, and South America.[5-8,15]

Correspondingly, 25% of maternal deaths occur antepartum, 26% intrapartum, and 49% postpartum.[9]

A Five-Step Approach to Critical Care in Pregnancy

We recommend a five-step systematic approach for the management of an obstetric patient in the ICU (Table 3).

Step 1: Is This a Medical or Obstetric Disorder?

Manifestations of medical disorders closely mimic obstetric conditions (Table 4). For example, preeclampsia, thrombotic thrombocytopenic purpura (TTP), and systemic lupus erythematosus may all present with hypertension, proteinuria, rising creatinine level, thrombocytopenia, and seizures. Similarly, acute viral hepatitis closely mimics acute fatty liver of pregnancy. The distinction is important because specific treatment is available for most medical disorders, whereas treatment options are limited for obstetric disorders. Prompt delivery reverses the progression of many obstetric disorders but may not alter the course of medical disorders.

Step 2: Is There Multiple Organ System Failure?

Multiple organ failure is common in obstetric and medical disorders; renal failure and coagulopathy in pregnancy deserve special mention. Acute renal failure is common because of altered systemic and renal hemodynamics in pregnancy.[8] Although acute tubular necrosis is the usual underlying pathology in nonobstetric patients, 7% to 20% of obstetric renal failure is due to acute cortical necrosis.[17-19] This form of severe ischemic renal damage occurs when shock is accompanied by microvascular thrombosis due to disseminated intravascular coagulation (DIC).[15,17,20] Women with acute cortical necrosis have anuria (< 100 mL urine/d) rather than oliguria and may be left with significant residual renal dysfunction requiring chronic dialysis.[17-20] Thrombocytopenia and DIC are present in many obstetric disorders, and all pregnant patients in the ICU should routinely undergo DIC screen; thromboelastography is used in some centers.[15]

Step 3: Is There a Risk to the Mother and Fetus if Pregnancy Is Continued?

Many obstetric disorders improve rapidly after delivery, and urgent delivery may be life saving. At times, urgent delivery is required for fetal distress, and sometimes the time required to stabilize maternal organ function may further compromise fetal outcome. The maternal risk from urgent delivery should be balanced against the risk to the fetus by delaying delivery. As a general principle, maternal well-being always takes precedence over that of the fetus. Occasionally, in complex situations like maternal brain death or terminal illness, the fetal condition assumes greater importance. Another situation involves the periviable period (22 to 24 weeks

TABLE 3] The Five-Step Approach to Critical Care in Pregnancy

Steps		Rationale
Step 1	Is this a medical or obstetric disorder?	Many obstetric disorders mimic medical disorders
		Treatment of the two differ completely
		Specific treatment available for many medical disorders; drugs of choice may differ in pregnancy
		Delivery may halt progression of most obstetric disorders but only few medical disorders
Step 2	Is there failure of multiple organ systems?	Almost all patients will have organ dysfunction
		Kidney injury, thrombocytopenia, and coagulopathy are commonest
		Support failing organ systems
		Fetal well-being and safety assume importance in selecting treatment options and targets
Step 3	Is there a risk to the mother and fetus if pregnancy is continued?	Maternal outcomes are better in some specific disorders if delivery is hastened; these should be identified.
		Fetal well-being is closely monitored
		Maternal survival takes precedence over fetal survival
Step 4	If delivery is to be hastened, vaginal delivery or Cesarean section? General or neuraxial anesthesia?	The decision-to-delivery time with mode of delivery and type of anesthesia and their associated risks must be balanced with the benefits
Step 5	What needs to be done to optimize patient for delivery?	Timely achievement of specific targets
		Hemodynamics, oxygenation, seizure control, thrombocytopenia, and biochemical and coagulation parameters must be optimized to ensure safe delivery

of gestation), when termination of pregnancy may benefit the mother but neonatal outcomes are extremely poor. In such circumstances the counsel of a medical ethicist should be sought.

Step 4: Early Delivery—Vaginal or Cesarean Section? General or Neuraxial Anesthesia?

The mode of delivery (vaginal vs cesarean section) is best determined by the indication for delivery and the maternal clinical status. Vaginal delivery may not be feasible in most emergency indications, as the duration of labor is unpredictable. Consequently, 70% of critically ill patients in the ICU are delivered by cesarean section.[3] Elective cesarean section is normally performed under regional anesthesia, given the increased risk of complications with general anesthesia in pregnancy.[21] However, in patients with shock, respiratory distress, seizures, and coagulopathy, the risk of hypotension and local hematoma with neuraxial anesthesia are significant.[21,22] General anesthesia may, therefore, be preferred in these women despite the high rate of intubation failure, crowded upper airways, and risk of aspiration of gastric contents.[21,23] Coordination between the intensivist, obstetrician, anesthesiologist, and neonatologist is vital in this situation.

Step 5: What Needs to Be Done to Optimize the Patient for Delivery?

The next step is to correct physiologic derangements and minimize any complications during delivery. Two doses of betamethasone (12 mg administered IM or IV, 12-24 h apart) facilitate fetal lung maturation in deliveries between 24 and 34 weeks.[24] Hypotension and hypovolemia should be corrected. Endotracheal intubation may be required for airway protection, mechanical ventilation, or both. Seizures and severe hypertension must be controlled. Anticoagulants are discontinued and appropriate blood products administered to correct anemia, thrombocytopenia, and coagulation abnormalities. Serum fibrinogen level $\geq$ 100 mg/dL and platelet count $>$ 50,000/μL should be maintained; platelet count $>$ 80,000/μL is required if neuraxial anesthesia is planned.[21,23] The timing of administration of blood products is critical in vaginal delivery, since labor may last for several hours. Platelet transfusion, heparin, and desmopressin should be avoided if TTP is suspected.

TABLE 4] Differential Diagnosis of Common Clinical Syndromes Seen in Obstetric Patients in the ICU

Clinical Syndromes	Obstetric Causes	Medical Causes
Jaundice	Acute fatty liver of pregnancy	Acute viral hepatitis
Coagulopathy	HELLP syndrome	Acute cholangitis with sepsis
Thrombocytopenia	HELLP syndrome	Malaria
Fever	Preeclampsia	Dengue fever
Elevated transaminases		Acute viral hepatitis
		Immune thrombocytopenic purpura
Seizures	Eclampsia	Epilepsy
Coma		Cerebral venous sinus thrombosis
		Intracranial hemorrhage
		Cerebral malaria
Acute pulmonary edema/ARDS during or immediately after delivery	Amniotic fluid embolism	Mitral stenosis
		Aspiration of gastric acid
Hypertension	Preeclampsia	Acute glomerulonephritis
Proteinuria		Systemic lupus erythematosus
Raised creatinine		Scleroderma renal crisis
Hypotension/shock in postpartum period	Hemorrhage	Pulmonary thromboembolism
	Amniotic fluid embolism	Peripartum cardiomyopathy
	Puerperal sepsis	Aortic dissection
	Postpartum pituitary necrosis (Sheehan syndrome)	
Thrombocytopenia	Preeclampsia	Systemic lupus erythematosus
Anemia	Postpartum HUS/TTP	Malaria
Renal dysfunction in postpartum period		

Although these syndromes are commonly caused by obstetric disorders, they can be closely mimicked by medical disorders as well. See Table 1 legend for expansion of abbreviations.

Conditions Unique to Pregnancy

In this section, we review some important obstetric disorders like hypertensive disorders in pregnancy, HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome, and amniotic fluid embolism, which cause significant organ failure. We also discuss some emerging obstetric conditions that were not so common in the past. Massive hemorrhage from adherent placenta is increasing because of the large number of pregnant women with scars from previous cesarean section. With complex fetal surgical interventions for congenital disorders, maternal complications from fetal interventions are increasing. Ovarian hyperstimulation syndrome is also becoming common because of treatment of infertility with assisted reproduction techniques.

Hypertensive Emergencies and Preeclampsia

Hypertension in pregnancy may occur as a spectrum of disorders, and its complications are a common indication for admission to the ICU.[1-8] Although the exact cause of hypertension in pregnancy is unknown, experts believe that the placenta is the focus for all maternal and fetal manifestations, because delivery is the only absolute cure.[25] Preeclampsia complicates up to 10% of all pregnancies. Patients with severe preeclampsia usually require ICU admission because of the high risk of developing multiple organ failure or seizures. Eclampsia represents the furthest end of the hypertensive spectrum and may develop before, during, or after labor.[26-28]

The onset of preeclampsia is heralded by visual symptoms, headache, upper abdominal pain, and spontaneous bruising.[26-28] Serum uric acid is decreased in normal pregnancy and uncomplicated chronic hypertension; hyperuricemia ($>$ 4.5 mg/dL) suggests development of superimposed preeclampsia.[26] Important manifestations and complications of preeclampsia are listed in Table 5.

Development of severe preeclampsia with organ dysfunction is an indication for urgent delivery after

TABLE 5] Major Manifestations of Severe Preeclampsia/Eclampsia and Their Clinical Significance

Manifestations	Clinical Significance
Proteinuria (>5 g/d), rising serum creatinine	Renal involvement; avoid diuretics as patients are usually hypovolemic
Epigastric or right upper quadrant pain, deranged liver enzymes (AST, ALT, LDH)	Mild liver dysfunction is common; has to be differentiated from HELLP syndrome and acute fatty liver of pregnancy; ultrasonography required to exclude liver hematoma
Spontaneous bruising, epistaxis, thrombocytopenia, deranged coagulation tests	Some hematologic dysfunction seen in almost all patients; DIC screen or thromboelastography required to decide about transfusion of blood products if obstetric intervention planned
Visual symptoms (scotomata, scintillations, diplopia), headache, drowsiness	Onset of CNS involvement—impending eclampsia (seizures), intracranial hemorrhage, posterior reversible encephalopathy syndrome; diffusion-weighted MRI or plain CT scan of the brain performed if seizures or neurologic deficits
Seizures	Most commonly eclampsia; intracranial pathologies (trauma, abscess, hemorrhagic/ischemic strokes), metabolic abnormalities (sodium, calcium, glucose levels), or drug overdose (alcohol withdrawal, cocaine abuse) to be excluded; alternative diagnoses common if seizures occur>72 h after delivery
Severe hypertension	BP>160/110 increases risk of intracranial hemorrhage; arterial pressure monitoring and parenteral drugs treatment required
Shock	Concealed retroplacental hemorrhage (placental abruption); liver rupture; postpartum hemorrhage
Pulmonary edema	Left ventricular failure; tocolytic-induced; ARDS due to aspiration; transfusion-associated acute lung injury; amniotic fluid embolism

ALT = alanine aminotransferase; AST = aspartate aminotransferase; DIC = disseminated intravascular coagulation; LDH = lactate dehydrogenase. See Table 1 legend for expansion of other abbreviations.

maternal stabilization. Laboratory tests may reveal thrombocytopenia, schistocytes, rising creatinine, or deranged liver function. Parenteral antihypertensives are used for severe hypertension (Table 6). Antenatal corticosteroids should be administered to promote fetal lung maturity between 24 and 34 weeks of gestation.[24,29,30] In pregnant women with severe preeclampsia before 32 weeks of gestation, seizure prophylaxis with IV magnesium sulfate is initiated.[31] Renal failure, although not an absolute contraindication, requires careful monitoring of serum magnesium level (therapeutic level, 4-7 mEq/L).[28] Worsening thrombocytopenia or liver and renal function require more frequent laboratory testing (q4-6h). In women with preeclampsia who are being managed expectantly, continuous electronic fetal monitoring and frequent fetal ultrasound scans are performed to monitor fetal well-being due to increased risk of abruptio placenta and stillbirth. Placental abruption can cause fetal compromise, maternal hemorrhagic shock, and DIC. Emergent delivery of the fetus is recommended in these situations.[28]

With the development of seizures, the focus of management shifts to protecting the airway, maintaining adequate oxygenation and ventilation, stopping the seizures, controlling hypertension, and ensuring stable hemodynamics. IV magnesium sulfate is administered for prevention and treatment of seizures in a dose of 4-6 g over 15 min followed by infusion of 1 to 2 g/h.[32,33] If IV access cannot be attained, 8 g may be given IM (4 g in each gluteal muscle) followed by 5 g every 6 h. For seizures refractory to magnesium therapy or if magnesium is contraindicated, a benzodiazepine (IV lorazepam 2-4 mg or diazepam 5-10 mg every 5 to 10 min to a maximum dose of 30 mg), phenytoin (15-20 mg/kg IV with a repeat dose of 10 mg/kg in 20 min), or levetiracetam (500 mg IV followed by 500 mg IV or po every 12 h) may be used.[28]

Fetal decompensation may occur during seizures. This frequently presents as fetal bradycardia or signs of placental insufficiency and usually resolves as the seizure dissipates. Placing the patient in the left lateral decubitus position, fetal scalp stimulation if rupture of membranes has occurred, and administration of terbutaline may help increase fetal heart rate. If the fetal condition fails to improve after the seizure, placental abruption should be suspected. Persistent maternal seizures after magnesium therapy are an indication for prompt delivery.[26,27]

TABLE 6] Antihypertensive Agents Used for Urgent BP Control in Pregnancy

Drug	Dose	Comments
Labetalol	10-20 mg IV, then 20-80 mg every 20-30 min to a maximum dose of 300 mg	Considered first-line agent in pregnancy
	Can also be infused at 1-2 mg/min IV	Contraindicated in patients with asthma, heart disease, or congestive heart failure
		FDA pregnancy category C
Hydralazine	5 mg IV or IM then 5-10 mg IV every 20-40 min	Higher doses associated with maternal hypotension, headaches, and fetal distress
	Can also be infused at a constant rate of 0.5-10 mg/h	FDA pregnancy category C
Nifedipine	10-20 mg po, repeated in 30 min if needed, then 10-20 mg every 3-6 h	Tachycardia and headaches may experience peripheral edema
		FDA pregnancy category C
Nicardipine	Continuous infusion at 3 mg/h and increase in 0.5 mg every 20 min to a maximum dose of 15 mg/h	Embryotoxicity occurred in rabbits with doses 24 times the MRHD, but not in rats with oral doses 8 times the MRHD. Nicardipine crosses the placenta (9% of maternal levels). Changes in fetal heart rate, neonatal hypotension, and neonatal acidosis may occur; incidence is comparable to other antihypertensives.
	Once BP control is achieved, titrate down	FDA pregnancy category C
Nitroglycerine	5 μg/min doubling every 5 min	More of a venodilator, requires arterial pressure monitoring
		Potential for methemoglobinemia with prolonged usage
		FDA pregnancy category C
Nitroprusside	0.25 μ/kg/min infusion, increase by 0.25 μ/kg/min every 5 min	Requires continuous BP monitoring with an arterial line
		Potential for cyanide toxicity with prolonged use restricts its usefulness
		FDA pregnancy category C

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are associated with fetal anomalies and are contraindicated in the preconception period and pregnancy (FDA pregnancy category D). The FDA is in the process of revising the pregnancy labeling guidelines for drugs. FDA = US Food and Drug Administration; MRHD = maximum recommended human dose.

HELLP Syndrome and TTP

HELLP syndrome, defined by hemolysis, elevated liver enzymes, and low platelets, is part of the spectrum of preeclampsia-eclampsia. Patients usually present in the third trimester or early postpartum with the typical signs and symptoms of preeclampsia, and it may be difficult to diagnose HELLP initially, as thrombocytopenia and mild elevation of transaminases may occur in preeclampsia even in the absence of HELLP syndrome.[34] In 15% of cases, HELLP syndrome is not associated with hypertension and must be differentiated from its imitators (TTP/hemolytic uremic syndrome [HUS], fatty liver of pregnancy, systemic lupus erythematosus, herpes hepatitis, and acute severe folate insufficiency).[28] Diagnosis is made primarily by laboratory findings. Microangiopathic hemolysis is defined by indirect hyperbilirubinemia, schistocytes on peripheral smear, low serum haptoglobin level, or elevated lactate dehydrogenase (LDH) value; elevated levels of aspartate aminotransferase $\geq$ 70 IU/L and platelets $<$ 100,000/μL are also essential for diagnosis.[34] Complications of HELLP include DIC, liver infarction or hemorrhage, renal failure, pulmonary edema, and increased risk for wound separation.[26,34] Patients with established HELLP syndrome should be delivered promptly after stabilization. Antenatal corticosteroids are administered between 24 and 34 weeks to enhance fetal lung maturity[24,29,30] but provide no proven benefit to the mother.[27] Close monitoring of BP, fluid balance, and oxygenation should continue until at least 48 h postpartum.[34]

HELLP syndrome may be confused with TTP, which usually occurs between 23 to 24 weeks but may occur

across all three trimesters. TTP/HUS with acute renal failure more commonly occurs postpartum.[35] Differentiating HELLP from TTP may be difficult, since both have varying degrees of microangiopathic hemolytic anemia, thrombocytopenia, neurologic impairment (the three primary criteria for diagnosis of TTP), as well as elevated creatinine and fever. In TTP, however, the LDH is usually higher and platelet count lower than in HELLP. Also, prothrombin time, partial thromboplastin time, and fibrinogen levels are usually normal in TTP, which is rare in HELLP, with platelet count < 50,000/mL. Plasma exchange is the mainstay of treatment of TTP in pregnancy, and delivery is reserved for severe cases with a viable fetus. Platelet transfusion is contraindicated in TTP, and this is one of the principal reasons to distinguish TTP from HELLP.

Abnormal Placentation, Massive Obstetric Hemorrhage, Massive Transfusion Protocol

Invasion of placental villi beyond the decidual layer into the uterine myometrium is termed placenta accreta.[36,37] Placenta increta refers to invasion into the myometrium, and placenta percreta is invasion through the myometrium into the serosa, surrounding tissues, or organs.[36,37] During delivery, the adherent placenta does not separate completely and causes severe hemorrhage and disseminated intravascular coagulopathy. A review by the American College of Obstetrics and Gynecology mentions that 90% of women with placenta accreta require blood transfusions and 40% require > 10 units of packed RBC.[36] Other complications include need for hysterectomy; surgical injury to the urinary bladder, bowel, or pelvic neurovascular structures; ARDS; transfusion reactions; electrolyte imbalance; and acute renal failure.[36,37]

The main risk factor for placenta accrete, presence of a uterine scar and prior cesarean delivery, is noted in 80% of cases.[36-39] Other risk factors include advanced maternal age, assisted reproductive therapy, multiparity, uterine surgery, submucous leiomyoma, thermal ablation, pelvic irradiation, and uterine artery embolization.[37] Diagnosis is usually by ultrasonographic demonstration of a thin myometrium (< 10 mm), large placental lakes, loss of the echolucent layer between the bladder and myometrium, and increased vascularity of the uterine serosa-bladder interface.[36,37] MRI may be used if ultrasound diagnosis is inconclusive and to demonstrate invasion into surrounding organs.[40]

Treatment is by planned preterm delivery by cesarean hysterectomy at 34 to 35 weeks in an experienced regional referral center with extensive blood banking and multidisciplinary capability.[37,41,42] The average anticipated blood loss in these patients is 1 L during a cesarean delivery and 2 to 5 L in a cesarean hysterectomy. Preoperative consultation with anesthesiology and blood bank personnel is key, given the potential for massive transfusion. Availability of other specialized services, such as urology, gynecologic oncology, and interventional radiology, may be warranted. Patients should be extensively counseled regarding the risks of hemorrhage, need for transfusion, possible intraoperative damage to bowel, bladder, ureters, or ovaries, as well as options for use of cell saver and directed blood donation. Preoperative placement of ureteral stents can reduce ureteral injury.[41]

As these patients have a propensity to bleed torrentially, an institutional massive transfusion protocol is vital. Massive transfusion, commonly defined as the need to administer > 10 units of packed RBCs in a 24-h period, correlates with loss of > 50% of the blood volume.[43] Effective resuscitation should include the ability to infuse blood products at a high rate (shock trauma infusion devices), maintenance of core temperature > 35°C, use of blood warmers, correction of hypocalcemia and hyperkalemia, and timely administration of component therapy.[44] Although data from military combat resuscitation support ratios of 1:1:1 for transfusion of RBCs:plasma:platelets, this has not been supported in the obstetric literature, and we prefer a 2:1:1 protocol (Michael Belfort, MBBCh; Jun Teruya, MD; Shiu-Ki Hui, MD; unpublished observations; 2014). The need for a coordinated multidisciplinary team approach with simulated patient scenarios cannot be overemphasized.

After acute bleeding has been controlled and the hemodynamics stabilized, a restrictive approach should be adopted to minimize complications of massive transfusion, which include acid-base derangements, electrolyte abnormalities, citrate toxicity, and transfusion-related acute lung injury.[44] In patients with prolonged hypotension, pituitary apoplexy (Sheehan syndrome) and renal failure should be anticipated.

Amniotic Fluid Embolism

Amniotic fluid embolism (AFE) or anaphylactic syndrome of pregnancy is a rare syndrome with a high mortality rate, estimated to occur between one to 12 per 100,000 deliveries.[45] Although originally believed to result from mechanical circulatory obstruction, exposure to fetal tissues, or both,[46,47] AFE is now believed

to involve an inflammatory anaphylactoid response to fetal antigens entering the maternal vasculature through a disruption in the maternal-fetal barrier. This results in a clinical triad of increased pulmonary and/or systemic vascular resistance, decreased left ventricular function, and coagulopathy, ultimately resulting in respiratory failure and cardiogenic shock.[47] Patients typically present with acute onset of right-sided cardiac failure, hypoxemia, respiratory distress, altered mental status, hypotension, coagulopathy, and sometimes sudden bradycardia and death during labor or immediately postpartum.[47,48] In the AFE registry, hypotension and nonreassuring fetal status were the two most common presentations; cardiac arrest was also common.[48] Predisposing conditions include rapid labor, meconium-stained amniotic fluid, older maternal age, postterm pregnancy, eclampsia, cesarean delivery, placental abruption, and hydramnios.[49]

Management of AFE is primarily supportive and focuses on (1) cardiopulmonary resuscitation, (2) judicious use of IV fluids with close hemodynamic monitoring, (3) supplemental oxygen or mechanical ventilation for respiratory failure, (4) administration of blood products for correction of coagulopathy, and (5) lateral displacement of the uterus during CPR.[47] Mortality rates exceed 60% in patients with classic presenting signs and increase to 90% if complicated by cardiac arrest; a significant number of survivors have neurologic sequelae from hypoxic-ischemic encephalopathy.[47,48]

Tocolytic Pulmonary Edema

Tocolytic agents are used for prevention of preterm delivery, primarily by inhibition of myometrial contractions. Evidence suggests that their use may result in pregnancy prolongation up to 48 h, permitting time for administration of antenatal corticosteroids.[29] Prolonged use has no proven neonatal benefit and may increase maternal risk of pulmonary edema. Magnesium sulfate is most commonly used for its dual effect of tocolysis and fetal neuroprotection in pregnancies < 32 weeks.[50] In some cases, subcutaneous terbutaline is the only effective tocolytic, especially following fetal surgical procedures or in the acute management of tetanic uterine contraction. Maintenance tocolysis is often continued with oral nifedipine or indomethacin.[50] Pregnancy-associated increase in cardiac output, blood volume, heart rate, and decreased colloid osmotic pressure predispose patients receiving tocolysis to develop pulmonary edema. Tocolytic-induced pulmonary edema is further aggravated by fluid overload.[50,51] It is treated with fluid restriction, discontinuation of the tocolytic agent, supplemental oxygen, respiratory support, and careful diuresis.[50,51] Echocardiography is performed to exclude a cardiac etiology.

Ovarian Hyperstimulation Syndrome

Ovarian hyperstimulation syndrome (OHSS) is a complication of supraphysiologic stimulation of the ovaries in an attempt to induce ovulation to facilitate pregnancy, to harvest eggs from a donor, or for in vitro fertilization.[52,53] It usually occurs following gonadotropin administration and occasionally with clomiphene or multiple pregnancies.[53] Occasionally OHSS may start with ovulation induction and continue or worsen if pregnancy occurs. Risk factors include asthenic build, age < 30 years, multigestational pregnancy, polycystic ovaries, excessive follicular response to stimulation drugs, and rapidly rising estradiol levels.[52,53]

The three main problems in OHSS are electrolyte disturbances, capillary leakage/third spacing of fluid, and hemoconcentration. These lead to complications such as hypotension, tachycardia, oliguria and renal failure, ascites, pleural effusions, ARDS, arterial or venous thrombosis, and stroke.[52-54] Patients with severe OHSS should be admitted to the ICU and may require abdominal paracentesis, thoracentesis, IV fluids to correct hypovolemia, and DVT prophylaxis.[53]

Fetal Mirror Syndrome

Fetal mirror syndrome (Ballantyne syndrome) is characterized by generalized edema and pulmonary edema in the mother in response to fetal hydrops, probably due to a systemic inflammatory response syndrome due to shedding of trophoblastic debris by the hydropic placenta.[55] Although initially described with rhesus alloimmunization, it may also occur with nonimmune hydrops, fetal arrhythmias, twin-twin transfusion syndrome, viral infections, fetal malformations, and placental or fetal tumors.[56] It usually presents between 16 and 34 weeks' gestation and mimics severe preeclampsia (elevated transaminases, pulmonary edema, hypertension, proteinuria, thrombocytopenia, and neurologic symptoms).[57] It may be distinguished from preeclampsia by the presence of a hydropic fetus on ultrasound.[57] Management of the underlying fetal condition usually results in reversal of maternal symptoms.[56,58] When no treatment is available, or when treatment does not result in rapid resolution of the maternal illness, delivery or pregnancy termination results in symptom resolution.[56]

Critical Illness in Fetal Surgeries

In utero fetal surgical interventions are increasingly being performed for some fetal conditions in specialized centers to stabilize the fetal condition (anemia or polycythemia, hydrops, cardiac failure, limb ischemia, cord strangulation) or prevent ongoing damage in a fetus with a congenital anomaly (meningomyelocele, bladder outlet obstruction, diaphragmatic hernia).[59] Other indications for fetal surgery include sacrococcygeal teratoma, amniotic bands, congenital cystic adenomatoid malformation, bronchopulmonary sequestration, twin-twin transfusion syndrome, and cardiac malformations.[59]

The techniques used for fetal surgery range from maternal laparotomy and hysterotomy (most invasive), endoscopic procedures with minimally invasive access laparoscopy assistance, and percutaneous ultrasound-guided procedures (least invasive).[60] Although the expected outcome is improved for the fetus, there are usually no direct maternal benefits, except perhaps in the treatment of mirror syndrome, where treatment of twin-twin transfusion syndrome or hydrops from other causes can reverse the maternal illness.[61] Significant maternal risk is involved in fetal surgery, often necessitating ICU admission. Tocolysis may be needed for several days to prevent preterm labor, and tocolytic-induced pulmonary edema is common. Maternal morbidity reported includes pulmonary edema (22%), blood transfusion (7%), preterm labor (27%), premature rupture of membranes (44.4%), chorioamnionitis (4.5%), placental abruption (6.2%),[60] increased risk of venous thromboembolism, and need for cesarean delivery for the index and all subsequent pregnancies.[59]

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CHEST™

Critical Illness in Pregnancy

Part II: Common Medical Conditions Complicating Pregnancy and Puerperium

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The first of this two-part series on critical illness in pregnancy dealt with obstetric disorders. In Part II, medical conditions that commonly affect pregnant women or worsen during pregnancy are discussed. ARDS occurs more frequently in pregnancy. Strategies commonly used in nonpregnant patients, including permissive hypercapnia, limits for plateau pressure, and prone positioning, may not be acceptable, especially in late pregnancy. Genital tract infections unique to pregnancy include chorioamnionitis, group A streptococcal infection causing toxic shock syndrome, and polymicrobial infection with streptococci, staphylococci, and *Clostridium perfringens* causing necrotizing vulvitis or fasciitis. Pregnancy predisposes to VTE; D-dimer levels have low specificity in pregnancy. A ventilation-perfusion scan is preferred over CT pulmonary angiography in some situations to reduce radiation to the mother's breasts. Low-molecular-weight or unfractionated heparins form the mainstay of treatment; vitamin K antagonists, oral factor Xa inhibitors, and direct thrombin inhibitors are not recommended in pregnancy. The physiologic hyperdynamic circulation in pregnancy worsens many cardiovascular disorders. It increases risk of pulmonary edema or arrhythmias in mitral stenosis, heart failure in pulmonary hypertension or aortic stenosis, aortic dissection in Marfan syndrome, or valve thrombosis in mechanical heart valves. Common neurologic problems in pregnancy include seizures, altered mental status, visual symptoms, and strokes. Other common conditions discussed are aspiration of gastric contents, OSA, thyroid disorders, diabetic ketoacidosis, and cardiopulmonary arrest in pregnancy. Studies confined to pregnant women are available for only a few of these conditions. We have, therefore, reviewed pregnancy-specific adjustments in the management of these disorders. CHEST 2015; 148(5):1333-1345

ABBREVIATIONS: CTPA = CT pulmonary angiography; DKA = diabetic ketoacidosis; ECMO = extracorporeal membrane oxygenation; LMWH = low-molecular-weight heparin; LV = left ventricle; MI = myocardial infarction; PE = pulmonary embolism; PRES = posterior reversible encephalopathy syndrome; RCVS = reversible cerebral vasoconstriction syndrome; UFH = unfractionated heparin

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This is the second of the two-part review on critical illness in pregnancy.[1] Medical conditions complicating pregnancy and puerperium are discussed.

ARDS in Pregnancy

Common causes of ARDS in pregnancy include obstetric disorders like amniotic fluid embolism, severe pre-eclampsia, and puerperal sepsis, and medical disorders like acute pyelonephritis, aspiration of gastric contents, and community-acquired pneumonia (Table 1).[2-4] ARDS is 10 times more common in gravidas.[5] Experimental data suggest that this may be because of a two-hit model in which increased proinflammatory cytokines due to pregnancy and parturition constitute the first hit, and infection, hemorrhage, or aspiration compose the second hit.[6] Experience from the 2009 influenza A(H1N1) pandemic has highlighted the challenges in managing severe ARDS in pregnancy.[7-9]

Noninvasive ventilation has been successfully used in some patients with ARDS in pregnancy.[10-12] More severe ARDS usually requires invasive ventilation using a lung-protective strategy; inability to maintain $Pao_2 > 70$ mm Hg and/or arterial oxygen saturation > 95% on supplemental oxygen or noninvasive ventilation or a worsening clinical course are indications for intubation and ventilation.[13] The plateau pressure target of < 30 cm H_2O (common in nonpregnant cases) may not be practical in obese patients or in late pregnancy, where intraabdominal pressure can increase physiologically up to 14 mm Hg.[2-4,13-15] Here, monitoring transpulmonary pressures may help in optimizing ventilator settings.[16,17] Fetal oxygenation is best represented by maternal Pao_2 rather than arterial oxygen saturation, and frequent blood gas analysis is required to maintain $Pao_2 > 70$ mm Hg, the level needed to maintain acceptable fetal acid-base balance.[18,19]

TABLE 1] Causes of ARDS in Pregnancy and Puerperium

Unique to Pregnancy	Not Unique to Pregnancy
Tocolytic-induced pulmonary edema	Aspiration
Eclampsia	Sepsis: pneumonia, urosepsis
Chorioamnionitis	2009 Influenza A(H1N1)
Amniotic fluid embolism	Varicella pneumonia
Trophoblastic embolism	TRALI, multiple transfusions
Abruptio placentae	Air embolism
Ovarian hyperstimulation syndrome[a]	Drug overdose
Endometritis	Fat emboli
Retained products of conception	Pulmonary contusion
Septic abortion	Inhalation injury
	Near drowning
	Pancreatitis

TRALI = transfusion-related acute lung injury.
[a]This may also rarely occur in nonpregnant women undergoing treatment of infertility.

The normal $Paco_2$ in pregnancy is 28 to 32 mm Hg with a maternal-fetal Pco_2 gradient of 10 mm Hg.[3] Permissive hypercapnia, acceptable in nonpregnant patients with ARDS, may have significant fetal effects.[2,4,13] Although mild hypercapnia increases uterine blood flow, $Paco_2 > 60$ to 70 mm Hg decreases uterine blood flow and increases fetal intracranial pressure.[20-23] At the same time, maternal hypocapnia may also lead to decreased uteroplacental blood flow and fetal alkalosis with a leftward shift of the oxygen dissociation curve, causing fetal hypoxia.[22-24]

When lung-protective ventilation strategies fail to maintain blood gas targets, alternative approaches, including prone positioning, extracorporeal membrane oxygenation (ECMO), and high-frequency oscillation, may be needed. Although prone positioning may be possible in early pregnancy, it has obvious limitations close to term because of its effect on the uterus, fetus, and intraabdominal pressure; lateral positioning may help by relieving aortocaval compression.[2,3] Large clinical trials using high-frequency oscillation as a salvage mode have not shown benefit in nonpregnant patients.[25,26] Case series suggest some benefit with ECMO in pregnant patients.[27,28] Anticoagulation treatment, usually required for ECMO, is believed to have contributed to death of three of six pregnant patients with 2009 influenza A(H1N1) treated with ECMO in one study[28]; lower intensity of anticoagulation improved maternal and fetal outcomes in a recent study.[27]

Termination of pregnancy by delivery is generally recommended in patients with ARDS due to obstetric causes.[4] For ARDS due to other causes, the usual obstetric indications should guide the timing and mode of delivery, as evidence that termination of pregnancy will improve maternal outcome is lacking.[2,3] In one series, six of 10 women with ARDS in the third trimester requiring mechanical ventilation were delivered for fetal distress; one fetus died, and three had perinatal asphyxia.[18]

Sepsis in Pregnancy and Puerperium

Sepsis is the fourth most common cause of death during pregnancy and the puerperium.[29-33] It accounts for 9.7% of maternal deaths worldwide in 2013[34] and 5% to 8% of

ICU admissions.[30-33] Genital tract infections form 50% of obstetric sepsis and usually occur postpartum.[35,36] Sepsis may also occur antenatally as chorioamnionitis or following invasive procedures (amniocentesis, fetal interventions) (Table 2).[36] Acute pyelonephritis and community-acquired pneumonia are other important causes of sepsis in pregnancy.[36,37]

Besides the classic systemic manifestations of sepsis, local manifestations include lower abdominal or perineal pain, vaginal discharge, frequency of urination, and diarrhea.[36] Generalized blanching erythema suggests streptococcal toxic shock syndrome, usually seen with group A *Streptococcus pyogenes* infection.[36] Blood cultures, vaginal/uterine swab, and a urine sample should be sent for culture. After delivery, both sides of the placenta should be cultured. Ultrasonography or CT scan of the pelvis may reveal retained products of conception, pyometra, or abscess formation in the myometrium, parametrium, or pelvis.[36,37] Intramyometrial gas pockets on a plain radiographs is an ominous sign highly suggestive of *Clostridium perfringens* ("gas gangrene") infection, which almost always demands immediate surgical intervention.[36] The surviving sepsis campaign guidelines provided a reasonable evidence-based strategy for the initial management of severe sepsis and can also be applied to pregnant patients, although much of the evidence is from studies in nonobstetric settings.[38] Prompt administration of antibiotics within 1 h of diagnosis is essential.[38,39]

The preferred antibiotics in puerperal sepsis are clindamycin with an aminoglycoside. Alternative agents include third-generation cephalosporins, a β-lactam plus β-lactamase inhibitor combination (amoxicillin-clavulanate or piperacillin-tazobactam).[36,37] Metronidazole may be added when β-lactams that are less effective against anaerobic bacteria are used. Carbapenems are preferred in infection with suspected extended spectrum β-lactamase-producing organisms. Choice of antibiotics in urinary infections and pneumonia are the same as in a nonpregnant patient (see Table 3 for US Food and Drug Administration category of anti-infective drugs).[36,37] Failure to respond to antibiotics should prompt a search for retained products of conception or spread of infection into the myometrium, pelvis, or peritoneum. Surgical intervention with source control is important in these cases. There should be a low threshold for suspecting abdominal compartment syndrome in late pregnancy. Presence of gas on imaging suggests *C perfringens* infection but can also be caused by *Bacteroides*, *Klebsiella*, and anaerobic streptococci. Rarely, polymicrobial infection with group A streptococci, *Staphylococcus aureus*, and *C perfringens* could result in necrotizing vulvitis or fasciitis characterized by intense erythema or bluish discoloration of the perineal skin, with edema and bulla formation.[37] Disproportionate pain and crepitus on palpation also point to this diagnosis.[37] Wide excision of the necrotic tissue and early institution of appropriate antibiotics are required. Group A streptococcal infection not responding to antibiotics may improve with IV IgG.[36] Severe sepsis may also have a deleterious effect on the fetus. Premature labor is common and many require urgent delivery by cesarean section for fetal distress. The fetus too may have an increased risk of bacterial infection. If chorioamnionitis is present, myometrial microabscesses

TABLE 2] Types of Genital Tract Infections, Predisposing Factors, and Causative Organisms in Obstetric Sepsis

Types of Genital Tract Infection	Predisposing Factors	Organisms Causing Genital Infections, %
Endometritis	Prolonged rupture of membranes	Group A *Streptococcus*, >50
Septic abortion	Repeated vaginal examinations	*Staphylococcus aureus*, 10-15
Chorioamnionitis	Cesarean section	*Escherichia coli*, 20-30
Uterine microabscesses	Fetal surgery during pregnancy	*Pseudomonas* species, 2-10
Pelvic abscess	Illegal abortion	*Streptococcus pneumoniae*, 2-5
Pyometra	Cervical cerclage	*Clostridium* species, 2-5
Gas gangrene	Retained products of conception	*Klebsiella* species, 2-5
Peritonitis	Obesity	*Acinetobacter* species, 2-5
Infected episiotomy of abdominal incision	Diabetes mellitus	
Perineal laceration	Older maternal age	
Necrotizing fasciitis and vulvitis	Conservative management of placenta accreta	
Pelvic septic thrombophlebitis	Delivery outside healthcare facility	

Adapted with permission from Sriskandan[36] and Barton and Sibai.[37]

TABLE 3] US Food and Drug Administration Pregnancy Categories of Commonly Used Antiinfective Agents

Pregnancy Category	Category B	Category C	Category D
Definition	Animal reproduction studies have failed to demonstrate a risk to the fetus, and there are no adequate and well-controlled studies in pregnant women.	Animal reproduction studies have shown an adverse effect on the fetus. There are no adequate and well-controlled studies in humans. The benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.
Drugs included	Erythromycin	Vancomycin	Aminoglycosides
	Azithromycin	Clarithromycin	Tetracyclines
	Penicillins	Trimethoprim	Tigecycline
	Cephalosporins	Sulphonamides	
	Nitrofurantoin	Fluoroquinolones	
	Metronidazole	Chloramphenicol	
	Amphotericin B	Colistimethate	
	Meropenem	Imipenem-cilastatin	
	Doripenem	Fluconazole	
	Daptomycin	Echinocandins	
	Fosfomycin		

The US Food and Drug Administration is in the process of revising the pregnancy labeling guidelines for drugs.

may form along the uterine incision. Extreme vigilance is required, since microabscess formation almost always requires hysterectomy.[36,37]

DVT/Pulmonary Thromboembolism

VTE is seven to 10 times more common in pregnancy than in age-matched nonpregnant women and occurs in five to 12 per 10,000 pregnancies.[40] DVT is three times more common than pulmonary embolism (PE).[41,42] The increased risk persists for up to 6 weeks postpartum and is believed to be due to progesterone-induced venodilation, compression of iliac veins by the gravid uterus, damage to pelvic veins during delivery, and the physiologic hypercoagulable state in pregnancy.[40] Other risk factors include previous VTE, thrombophilia, BMI > 25, immobilization, assisted reproduction, puerperal sepsis, preeclampsia, and cesarean delivery (Table 4).[40-42]

Left leg DVT occurs in 85% of cases due to compression of the left iliac vein by the right iliac artery and the uterus. DVT manifests as unilateral or asymmetric edema, calf pain, and palpable cordlike veins.[40,42] Diagnosis of DVT in pregnancy can be challenging, as edema may occur due to other causes. Testing D-dimer levels is not recommended, as D-dimer levels increase progressively in normal pregnancy,[40,44] and have low specificity (6% to 23%) in pregnancy.[44]

Compression ultrasonography is the initial test for DVT.[44,45] Its yield is higher in women with symptomatic DVT; false-negative rate is high in pelvic vein thrombosis and in women without signs of DVT.[44] If negative, the test should be repeated after a week.[45] For the diagnosis of pulmonary embolism, a chest radiograph should be performed initially with abdominal shielding.[44] In women with severe hypoxemia or hemodynamic compromise, CT pulmonary angiography (CTPA) is performed as the next investigation.[40] In less severe cases with a normal chest radiograph, a ventilation-perfusion scan is recommended instead of CTPA, as it exposes the mother's breasts to less carcinogenic radiation than CTPA, with almost equivalent radiation to the fetus.[44] When clinical suspicion is high and the ventilation-perfusion scan is nondiagnostic or chest radiograph shows a pulmonary lesion, CTPA is performed.[44] Circumferential abdominal shielding reduces fetal radiation exposure during CT imaging, but not during scintigraphy, where accumulation of isotope in the mother's urinary bladder is the main contributor to fetal exposure.[46]

Guidelines for treatment of VTE in pregnancy recommend low-molecular-weight heparin (LMWH) in preference to unfractionated heparin (UFH) or oral vitamin K antagonists (Table 5).[43,45] IV UFH may, however, be preferred in women with morbid obesity,

TABLE 4] Indications for Postpartum Thromboprophylaxis, Especially Following Cesarean Section

Risk Category	Risk Factors
Major risk factors	
Presence of one or more risk factors suggests > 3% risk of postpartum VTE	Immobility (strict bed rest for > 1 wk in the antepartum period)
	Postpartum hemorrhage > 1,000 mL with surgery
	Previous VTE
	Preeclampsia with fetal growth restriction
	Thrombophilia
	Antithrombin III deficiency
	Factor V Leiden (homozygous or heterozygous)
	Prothrombin G20210A (homozygous or heterozygous)
	Medical conditions
	Systemic lupus erythematosus
	Heart disease
	Sickle cell disease
	Blood transfusion
	Postpartum infection
Minor risk factors	
Presence of two or more risk factors suggests > 3% risk of postpartum VTE	BMI > 30 kg/m^2
	Multiple pregnancy
	Postpartum hemorrhage > 1 L
	Smoking > 10 cigarettes/d
	Fetal growth restriction (gestational age + sex-adjusted birth weight < 25th percentile)
	Thrombophilia
	Protein C deficiency
	Protein S deficiency
	Preeclampsia

Adapted with permission from Bates et al.[43]

renal dysfunction, hemodynamic instability, and high risk of bleeding; anticoagulation should be monitored by appropriate tests.[40,43,47] Thrombolysis (100 mg of recombinant tissue plasminogen activator infused IV over 2 h) should only be used for limb-threatening DVT or massive PE with severe hypoxemia or hemodynamic compromise (grade 3C)[45]; thrombolysis in right ventricular dysfunction without hypotension is controversial.[40,45] Ovarian vein thrombosis affects women postpartum most commonly after cesarean section. Antibiotics should be started in such patients.[45] Women on long-term LMWH therapy during pregnancy should be switched to UFH at 36 to 37 weeks of gestation. UFH should be stopped at the onset of labor or 24 h before planned cesarean section.[40,43,45] LMWH or oral vitamin K antagonists should be given for 6 weeks postpartum or for 3 months postpartum after diagnosis of DVT/PE.[43]

Aspiration

First described by Mendelson[48] in 1946, aspiration-induced lung injury in pregnancy is an underdiagnosed entity and is a major risk factor for the development of ARDS.[49] It can occur as microaspiration or large-volume aspiration of gastric secretions, food particles, oropharyngeal bacteria, or blood. A well-recognized complication of general anesthesia, its risk is higher in pregnancy because of slower gastric emptying and reduced esophageal sphincter tone. Other risk factors include altered mental status, drug ingestion, seizures, esophageal motility disorders, gastroesophageal reflux, bowel obstruction, and obesity.[50]

Pulmonary consequences of aspiration occur into two phases and depend on the volume, pH, and particle size of the aspirated material. The first phase occurs

TABLE 5] Antithrombotic Therapy and Thromboprophylaxis in Pregnancy and Postpartum Period

Clinical Situation		Recommendations (Grade of Evidence)
Thromboprophylaxis		
Planning pregnancy	On vitamin K antagonists for prior VTE	Frequent pregnancy tests
		Switch to LMWH when test positive (2C)
Becomes pregnant	On vitamin K antagonist for prior VTE	LMWH preferred over vitamin K antagonist in
		First trimester (1A)
		Second and third trimester (1B)
		Late pregnancy, nearing delivery (1A)
During pregnancy	VTE prophylaxis	LMWH preferred over UFH (1B)
		Avoid fondaparinux and parenteral direct thrombin inhibitor except heparin allergy/HIT (2C)
		Avoid oral direct thrombin or anti-Xa inhibitors (1C)
Ovarian hyperstimulation syndrome	Before or during pregnancy	LMWH prophylaxis for 3 mo after resolution of the syndrome (2C)
Delivery	Delivery by cesarean section:	
	No risk factors for DVT	No thromboprophylaxis (1B)
	Significant risk of DVT (see Table 4)	LMWH or mechanical prophylaxis while in hospital if LMWH contraindicated (2B)
	Very high risk	LMWH + mechanical prophylaxis (2C)
Delivery	Delivery by any mode, very high risk of VTE	Thromboprophylaxis for 6 wk postdelivery (2C)
Treatment of VTE/mechanical heart valves		
Planning pregnancy	On vitamin K antagonists	Frequent pregnancy tests (2C)
		Switch to LMWH when test positive
Becomes pregnant	On vitamin K antagonist	LMWH preferred over vitamin K antagonist in
		First trimester (1A)
		Second and third trimester (1B)
		Late pregnancy, nearing delivery (1A)
During pregnancy	Choice of pharmacologic agent	LMWH preferred over UFH (1B)
		Vitamin K antagonists (1A)
		Avoid fondaparinux and parenteral direct thrombin inhibitor except heparin allergy/HIT (2C)
		Avoid oral direct thrombin or anti-Xa inhibitors (1C)

(Continued)

TABLE 5] *(continued)*

Clinical Situation		Recommendations (Grade of Evidence)
	Duration of treatment	Minimum 3 mo (2C)
		At least 6 wk postpartum (2C)
		LMWH or vitamin K antagonist can be used postpartum (2B)
	Planned delivery	Discontinue LMWH 24 h before induction of labor or expected time of neuraxial anesthesia for cesarean section (1B)
Mechanical heart valves	During pregnancy	Adjusted dose LMWH bid throughout pregnancy—monitor anti-Xa activity (1A)
		Adjusted dose UFH throughout pregnancy administered subcutaneously bid—monitor aPTT (1A)
		UFH or LMWH until 13th week, then oral vitamin K antagonists until close to delivery, then UFH or LMWH until delivery (1A)
	During pregnancy, very high risk of thromboembolism (eg, older-generation valve in mitral position, prior thromboembolism)	Vitamin K antagonists throughout pregnancy, replaced by LMWH or UFH close to delivery (2C)
		Consider adding low-dose aspirin (2C)
Lactating women	Want to continue breast feeding	Can continue following:
		Warfarin, acenocoumarol (1A)
		UFH (1A)
		LMWH (1B)
		Danaparoid (1B)
		r-Hirudin (1B)
		Recommend use of alternatives to following:
		Oral direct thrombin inhibitors (1C)
		Oral factor Xa inhibitors (1C)
		Fondaparinux (2C)

aPTT = activated partial thromboplastin time; HIT = heparin-induced thrombocytopenia; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin. Recommendations are based on the American College of Chest Physicians guidelines in Bates et al.[43]

immediately and involves intense coughing and bronchospasm.[49] Over the next 6 to 12 h there can be progress to a second phase of inflammation, increased capillary permeability, loss of surfactant leading to atelectasis, pulmonary infiltrates, hypoxemia, and in some cases ARDS. A few patients develop bacterial necrotizing pneumonia leading to lung abscesses.[49]

Management consists of lateral positioning of the patient, oropharyngeal suctioning, and elevation of the head of bed.[49] The decision to intubate depends on the degree of hypoxia, work of breathing, and mentation. Nebulized bronchodilators may help relieve wheezing; bronchoscopic suctioning may help in large volume particulate aspiration. Antibiotics are not necessary for gastric aspiration but may be used if the diagnosis is not clear. Steroids are not recommended for aspiration pneumonitis.[49]

Neurologic Emergencies in Pregnancy

Common neurologic emergencies in pregnancy include acute severe headache, seizures, hypertensive encephalopathy, altered mental status, and acute neurologic deficits. Severe headache during late pregnancy should prompt an evaluation for preeclampsia. Migraine usually improves during pregnancy because of estrogens and worsens after delivery.[51,52] Visual blurring, diplopia, or scotomata, usually seen in migraine, also occur in more serious conditions like severe preeclampsia, posterior reversible encephalopathy syndrome, stroke, pituitary apoplexy, and orbital hemorrhage.[51,53] Orbital hemorrhage, a rare complication of pregnancy, may occur in the first trimester due to hyperemesis gravidarum (retching, vomiting) or during labor due to straining.[51] Stroke is the most common neurologic disorder leading to ICU admission and is responsible for 20% of deaths in pregnancy.[53,54] Ischemic strokes are the commonest (four to 11 per 100,000 deliveries) followed by intracranial hemorrhage (3.7 to nine per 100,000), subarachnoid hemorrhage (2.4 to seven per 100,000), and cerebral venous sinus thrombosis (0.7 to 24 per 100,000).[51] The risk of stroke is highest in late pregnancy and puerperium. Risk factors include older maternal age, hypertension, dehydration, systemic lupus erythematosus, thrombophilia, sickle cell anemia, heart disease, and diabetes mellitus.[51-54]

Diagnostic imaging should be promptly performed for suspected stroke. Plain or contrast-enhanced CT scan of the brain with abdominal shielding is safe in pregnancy, as is an MRI scan.[51] Gadolinium contrast for MRI should be avoided (US Food and Drug Administration pregnancy category C), whereas iodinated radiologic contrast is safe (category B).[44,51] Thrombolysis with recombinant tissue plasminogen activator for acute ischemic stroke is safe in pregnancy, as it does not cross the placenta; preeclampsia, however, is a relative contraindication.[52,54] In aneurismal subarachnoid hemorrhage, the benefits of endovascular coiling outweigh the hazards of ionizing radiation and periprocedure anticoagulation.[52]

Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by reversible multifocal cerebral vasospasm occurring within a week of delivery.[51,55] Manifestations include thunder-clap headache, transient focal deficits, fluctuating visual symptoms, and sometimes seizures. Imaging reveals focal vasoconstriction of cerebral arteries, areas of infarction, and sometimes posterior reversible encephalopathy syndrome (PRES) or convexity subarachnoid hemorrhage.[51,54,55] Treatment with nimodipine has met with variable success[55]; mortality in RCVS is $< 1\%$.

PRES is a reversible vasogenic subcortical edema seen predominantly in the parietal and occipital lobes (but may occur anywhere in the brain), often associated with hypertension in pregnancy. It manifests as headache, visual impairment, and altered mental status and sometimes as seizures and coma.[51,53,55]

New-onset seizures during pregnancy should be assumed to be due to eclampsia or intracranial hemorrhage until proven otherwise.[51,53] Other causes of seizures in pregnancy included cerebral venous sinus thrombosis, RCVS, PRES, thrombotic thrombocytopenic purpura, and cerebral lupus.[51,53] Breakthrough seizures may occur in women with epilepsy nearing term due to altered pharmacokinetics of antiepileptic drugs. Seizure risk is highest during labor and the subsequent 24 h, probably due to failure to take oral antiepileptic medications, impaired absorption, or sleep deprivation.[56,57] In women with status epilepticus, metabolic causes like hypoglycemia, hyponatremia, hypocalcemia, and Wernicke encephalopathy must be excluded.[53,56] Seizure control is achieved with IV lorazepam and a loading dose of fosphenytoin; IV magnesium sulfate is the drug of choice for eclamptic seizures.[56,57]

Obesity and OSA

An estimated 36% of adult women in the United States have a BMI > 30 kg/m^2,[58] including a significant number of women of childbearing age.[59] Louis et al[60] prospectively studied pregnant women with a BMI > 30 kg/m^2 and found OSA in 15.4%, with $> 50\%$ having a moderate to severe range apnea-hypopnea index. Women with OSA had a higher mean BMI, were more likely to have a

cesarean delivery than the control group (65% vs 33%), and were also more likely to develop preeclampsia (42% vs 17%). Although preterm birth rate was similar, OSA was associated with more neonatal ICU admissions (46% vs 18%) and hyperbilirubinemia (58% vs 30%).[60] A recent meta-analysis found significant associations between sleep-disordered breathing and gestational hypertension, preeclampsia, and gestational diabetes.[61] The prevalence of OSA increases from 10.5% during the first trimester to 26.7% in the third trimester.[62] Rising levels of estrogen during pregnancy induce hyperemia, nasopharyngeal mucosal edema, and vasomotor rhinitis, which contribute to narrowing of upper airways. Decreased functional residual capacity and caudal traction on the trachea and pharynx during inspiration enhance pharyngeal collapsibility. Small airway closure can lead to ventilation-perfusion mismatch, which further reduces maternal oxygen reserves.[62] Table 6 outlines the perinatal complications of OSA parturients with obesity.[63]

Obese parturients need careful airway assessment, since failed intubation is eight times more common than in the nonobese parturient. Nearly 90% of parturients who experienced a failed intubation had a BMI >30 kg/m^2.[63] Regional anesthesia too may pose challenges due to problems with positioning, identification of landmarks, depth of the epidural space, and epidural catheter dislodgement.[63] Parturients with moderate/severe OSA receiving general anesthesia should recover in a postanesthesia care unit with close monitoring. Perioperative CPAP/bilevel pressure ventilation may reduce maternal morbidity. DVT prophylaxis and early ambulation are recommended.

Cardiac Disease in Pregnancy

Cardiac disorders accounted for 18.3% of ICU admissions in pregnancy and 36% of maternal deaths in a statewide study from Maryland.[32] Physiologic increase in blood volume, cardiac output, and tachycardia and decreased vascular resistance in pregnancy adversely affect preexisting cardiac diseases.[64-66] The World Health Organization classifies heart disease into four pregnancy risk classes.[65,67] Risk class 3 indicates increased risk of maternal mortality or severe morbidity and includes patients with a mechanical prosthetic valve, some complex congenital heart diseases, and aortic dilatation of 40 to 45 mm with Marfan syndrome or 45 to 50 mm with a bicuspid aortic valve.[65,67] Pregnancy is contraindicated in risk class 4 because of extremely high risk of maternal mortality or severe morbidity.[65] This class includes pulmonary hypertension from any cause, left ventricular (LV) dysfunction (LV ejection fraction $<30\%$, New York Heart Association stage III/IV), previous peripartum cardiomyopathy with residual ventricular dysfunction, severe mitral or aortic stenosis, severe coarctation of the aorta, and aortic dilatation >45 mm in Marfan syndrome or >50 mm with bicuspid aortic valve.[65,67]

Pulmonary arterial hypertension is associated with a mortality of 17% to 33% due to disease progression, right ventricular failure, and/or pulmonary thrombosis, especially in the last trimester and puerperium. Supplemental oxygen, IV prostacyclin or aerosolized iloprost, phosphodiesterase inhibitors, and anticoagulation treatment may help.[65,68] Pulmonary artery catheterization is avoided since its usefulness has not been demonstrated, and there is additional risk of pulmonary artery rupture.[65] Mothers with ascending aortic dilatation in Marfan syndrome have increased risk of aortic dissection; use of β-blockers may reduce this risk. Increasing aortic dilatation in the third trimester is an indication for urgent delivery by cesarean section followed by surgical repair.[65]

Pregnant women with severe mitral stenosis may develop recurrent pulmonary edema and atrial fibrillation, and women with severe aortic stenosis may develop heart failure or fatal arrhythmias.[65,66] Treatment consists of restricting activity, diuretics, β_1-selective blockers or calcium channel blockers for rate control in atrial fibrillation, and anticoagulation to prevent thromboembolism in chronic atrial fibrillation.[65,66] Balloon valvotomy with abdominal shielding is safe and effective in selected cases with severe mitral or aortic stenosis after 20 weeks of pregnancy.[66] In aortic stenosis with resistant heart failure, early cesarean delivery followed by valve replacement must be considered.[65] Patients with prosthetic valves may develop valve thrombosis in pregnancy despite use

TABLE 6] OSA: Maternal and Fetal Complications

Maternal Complications	Fetal Complications
Recurrent early miscarriage	Fetal macrosomia
Spontaneous abortions	Shoulder dystocia
Pregnancy-induced hypertension	Unexplained stillbirth
Gestational diabetes	
Risk of aspiration	
Preterm delivery	
Risk of cesarean section	
Thromboembolism	

Adapted with permission from Ankichetty et al.[63]

of UFH or LMWH; thrombolysis is useful for hemodynamically significant valve thrombosis.[65]

Acute myocardial infarction (MI) is rare (six in 100,000 deliveries) and usually occurs in pregnant women > 40 years of age due to coronary artery stenosis (40%), spontaneous dissection (27%), thrombosis (8%), or spasm (2%), with mortality of 11%.[65,69,70] As coronary artery dissection is a common cause of MI, percutaneous coronary revascularization with bare-metal stent insertion is preferred over thrombolysis for ST elevation MI in pregnancy.[64,65,69] Thrombolysis may be performed if angioplasty is not available. The safety of drug-eluting stents in pregnancy is unproven.[65,69]

Peripartum cardiomyopathy occurs in one is 2,000 pregnancies[64] and is characterized by heart failure in the last month of pregnancy or within 5 months postpartum.[71,72] Risk factors include black race, multiparity, multifetal pregnancy, older age, teenage pregnancy, preeclampsia, hypertension, and diabetes mellitus.[64,65,71,73] LV function normalizes within 6 months after delivery in 50% of women, but the cardiomyopathy recurs in 30% to 50% of subsequent pregnancies.[65,71] Women with residual LV dysfunction have 85% 5-year mortality.[71] Preliminary studies suggest that bromocriptine may help in recovery of cardiac function in peripartum cardiomyopathy.[72]

Thyroid Disease in Pregnancy

Hyperthyroidism is seen in 1% to 2% of pregnant patients, mainly due to Graves disease.[74,75] Postpartum thyroiditis occurs in 5% to 7% of patients.[74] The hyperdynamic circulation of normal pregnancy makes the diagnosis of hyperthyroidism challenging. Elevated serum-free T4 level with decreased thyroid-stimulating hormone confirms diagnosis.[74-76] Transient neonatal hypothyroidism or hyperthyroidism occurs in 1% to 3% of infants due to crossing of the thyroid receptor antibodies. Antithyroid treatment with thioamides during pregnancy may also cause hypothyroidism or goiter in < 4% of neonates. Thyrotoxic crisis in pregnancy may not present with the classic signs of fever, tachycardia, and hypertension.[76,77] It may mimic severe hyperemesis gravidarum in early pregnancy and manifest as sweating, restlessness, diarrhea, or cardiac failure in later pregnancy.[74,78,79] Management consists of treating the precipitating cause, thyroid hormone control by propylthiouracil, and control of the hypermetabolic state using β-blockers and dexamethasone.[74,75]

Diabetic Ketoacidosis in Pregnancy

Pregnancy is a diabetogenic state, resulting from insulin resistance, increased ketogenesis, lipolysis, and free fatty acids. The incidence of diabetic ketoacidosis (DKA) in pregestational patients with diabetes during pregnancy is 1.7% to 22%.[80] Although the maternal mortality from DKA has reduced to < 1%, even a single episode of DKA during pregnancy carries a perinatal mortality of 9% to 35%.[80,81] In pregnancy, DKA can be seen at relatively low glucose levels, as low as 180 mg/dL. DKA may be the first manifestation of diabetes in pregnancy in up to one-third of patients. Other causes include noncompliance with insulin therapy (40%) and sepsis (20%).[81] Management is similar to nonpregnant patients with DKA, including volume replacement; monitoring and correction of serum phosphate, potassium, and magnesium; clearance of ketosis; treatment of the precipitating cause; and close monitoring of mother and fetus.[80,81]

Cardiopulmonary Arrest in Pregnancy

Although a rare event, with an estimated incidence of one in 30,000 deliveries, a cardiopulmonary arrest in a pregnant patient poses unique challenges.[82,83] Common causes of sudden cardiac arrest in pregnancy are VTE, hemorrhage, pregnancy-induced hypertension, amniotic fluid embolism, trauma, and iatrogenic and preexisting cardiac disease.[83,84] BEAU-CHOPS (bleeding, embolism, anesthetic complications, uterine atony, cardiac disease, hypertensive disease, other, placenta [abruption, previa], sepsis) is a mnemonic suggested by the American Heart Association to remember the causes of sudden cardiac arrest in pregnancy.[83] Severe hypocalcemia and hyperkalemia may lead to cardiac arrest in women who have received massive transfusion for postpartum hemorrhage.[82] Pneumothorax and pericardial effusion should be ruled out by bedside ultrasonography.[83]

Salient points for advanced cardiac life support in this special situation include lateral displacement of the uterus during CPR and ruling out common causes of cardiopulmonary arrest in a nonpregnant patient, such as pneumothorax and pericardial effusion, by bedside ultrasonography.[83-85] Calcium gluconate is administered if magnesium toxicity is suspected as a cause of cardiac arrest and IV infusion of 20% lipid emulsion to adsorb the lipid soluble anesthetic if bupivacaine toxicity is suspected.[86] An important principle of resuscitating a pregnant woman beyond 20 weeks' gestation is delivery of the fetus by perimortem cesarean section if return of spontaneous circulation does not occur within 4 min. The fetus should be delivered in the next 1 min, and, therefore, the resuscitation team must include a trained obstetrician.[82-85] Neurologic outcome of the fetus and the hemodynamic status of the mother seem to be better served by prompt delivery of the fetus within 5 min of

cardiopulmonary arrest. The decision to deliver the fetus via postmortem cesarean section when resuscitative efforts have been unsuccessful, and the possibility of giving organ support to a brain-dead mother, are ethically complex, and one needs to be sensitive to religious, cultural, and other considerations while providing support to the family.

Conclusions

Medical disorders are important causes of morbidity and mortality in pregnancy and puerperium. Outcome studies suggest that critically ill obstetric patients with medical disorders have high severity of illness scores on ICU admission.[29,31,87] Paradoxically, almost all studies have shown that maternal survival is relatively better than in nonpregnant women with a comparable severity of illness.[31,87,88] Few studies have looked at fetal outcomes. Cartin-Ceba et al[89] studied 93 pregnant women in the ICU with medical disorders; 50% had adverse fetal outcomes, with 18 spontaneous abortions, 14 fetal deaths, and 49% premature deliveries; 10 neonates required ICU admission. Gestational age, shock, and need for blood transfusion in the mother predicted poor fetal outcome.[89]

Considerable efforts are being made to detect complications in pregnancy early, before the onset of serious organ dysfunction. One such strategy recommended by the Confidential Inquiry into Maternal and Child Health in UK is use of a modified early obstetric warning system (MEOWS).[90] Oral temperature, BP, heart rate, respiratory rate, oxygen saturation, level of consciousness, and pain scores are recorded periodically in hospitalized pregnant women.[91] A single markedly abnormal observation (red trigger), or two simultaneous mildly abnormal observations (yellow triggers) should prompt urgent medical assessment to exclude a developing critical illness.[91] Widespread adoption of this approach may reduce maternal and fetal morbidity and mortality.

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