Critical illness in pregnancy: An overview

Said H. Soubra, MD; Kalapalatha K. Guntupalli, MD

Objectives: **To provide an overview of the critical illnesses that afflict the pregnant patient.**

Design: **A comprehensive review of the literature was performed with Pubmed Medline using medical subject headings of pregnancy, critical care, epidemiology, prognostic score, dyspnea, fever, and jaundice.**

Results: **Although pregnant women constitute a small number of admissions to an intensive care unit, they pose a challenge to the health care team. The physiological changes that occur in pregnancy stress and limit the compensatory response required to adapt to a superimposed acute illness. Although a number of conditions are uniquely associated with pregnancy, other medical conditions may complicate the course of pregnancy. The pregnant state also increases susceptibility to a number of illnesses. In this overview, we reviewed the epidemiology and different clinical presentations of critical illness in a pregnant patient.**

Conclusions: **The critically ill pregnant patient presents a challenge to the critical care physician due to unique physiology and specific medical disorders in this population. (Crit Care Med 2005; 33[Suppl.]:S248–S255)**

KEY WORDS: epidemiology; prognostic score; dyspnea; jaundice; fever; pregnancy

Critically ill obstetric patients are significantly different from the average patient admitted to the medical intensive care unit (ICU). They present a challenge to the critical care physician due to their unique physiology and the specific medical disorders that occur during pregnancy and the peripartum period. The physiologic changes that occur in the pregnant state in several systems, including the cardiovascular, respiratory, renal, hematologic, and endocrine systems, stress the reserve of the body and may compromise responses needed to combat disease state. Furthermore, in addition to the common admitting diagnoses to a medical ICU, these patients present with disorders peculiar to pregnancy, including peripartum hemorrhage, pregnancy-induced hypertensive disorders, liver failure, embolic disorders, and puerperal infections (1). The challenges faced in the treatment of this patient population are even greater due to the fact that two lives are endangered simultaneously. In this article, we give an overview of the critical illnesses that afflict the obstetric patient. A comprehensive list of the conditions that may require admission to the ICU in pregnancy or within 6 wks of delivery is featured in Table 1.

From the Section of Pulmonary and Critical Care Medicine, Baylor College of Medicine (SHS, KKG); Michael E. Debakey Veterans Affairs Medical Center, Houston, TX (SHS); and Ben Taub General Hospital, Houston, TX (KKG).

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Epidemiology

The prevalence of obstetric patients requiring critical care ranges from 100 to 900 per 100,000 gestations (2–4). Estimated maternal mortality differs greatly between developed and developing countries. Whereas maternal mortality in year 2000 ranged between 6 and 24 deaths per 100,000 lives births in developed regions, it continues to be significantly elevated in developing regions, accounting for 55–920 deaths per 100,000 live births (Table 2) (5). Health care systems in developed countries have concentrated on improving the quality and access to antenatal care, thereby detecting complications early and providing expeditious care, resulting in improved outcome. Several pregnancy-related illnesses are reversed with early delivery of the fetus. This has been accomplished successfully with improvement in neonatal intensive care for preterm births (6). In contrast, the lack of antenatal and neonatal care, added to the social and economic factors in developing countries, results in a significantly higher mortality rate (7–9).

Risk Factors for Obstetric Disorders

Patient-Specific Risk Factors. There are patient-specific factors that increase the risk of developing certain diseases during pregnancy, as well as factors that influence the risk of admission to the ICU. Several retrospective studies have analyzed the effect of racial differences on both outcome and risk of admission to the ICU. Ethnic minorities, recent immigrants, and people of low socioeconomic status have been associated with worse outcome (10–12). Panchal et al. (10), in a retrospective analysis of 1,023 ICU admissions, showed that age, race, hospital type, volume of deliveries, and source of admission were all associated with risk of admission to the ICU. He also showed that African-American race and hospitals with high delivery volume had higher mortality rates. In a large study comparing patients from two publicly funded hospitals, one in Houston, TX, and the other one in Mumbai, India, Munnur et al. (13) showed a ten-fold increase in mortality rate in the Indian hospital. The patients in the Indian hospital were sicker, with a higher Acute Physiology and Chronic Health Evaluation (APACHE II) scores, received less antenatal care, and presented later to the hospital. This study also showed a difference in the admitting diagnoses as well as in the type of organ dysfunction (13).The interventions done were also different between the groups, indicating differences in admitting diagnosis and practice patterns (Tables 3 and 4).

Disease-Specific Risk Factors. Obstetric patients admitted to the ICU fall into

Table 1. Conditions that may require intensive care during pregnancy or within 6 wks after delivery

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

HELLP, hemolysis, elevated liver enzymes, and low platelets; ARDS, acute respiratory distress syndrome; HUS, hemolytic uremic syndrome; TTP, thrombotic thrombocytopenic purpura.

Table 2. Estimated regional maternal mortality in year 2000

Developed		Developing	
Region	Rate (Deaths/100,000 Deliveries)	Region	Rate (Deaths/100,000 Deliveries)
Overall	20	Overall	440
Europe	24	Africa	830
United States	17	Northern Africa	130
Canada	6	Sub-Saharan Africa	920
Japan	10	Asia	330
Australia	8	Eastern Asia	55
New Zealand	7	Southeast Asia	210
		South central Asia	520
		Western Asia	190
		Latin America and the Caribbean	190
		Oceania	240

Adapted from Ref. 5.

two categories: patients with obstetric disorders and pregnant patients with primarily medical disorders. The majority of patients (50–80%) are admitted to the ICU for obstetric disorders (13, 6). No differences have been seen in the propensity for a certain admitting obstetric disorder in different regions of the world (13, 5). In addition, patients with primarily obstetric disorders tend to have a better overall prognosis. On the other hand, the admitting diagnoses in patients with primarily medical disorders are variable, depending on the geographical location of the patient. Munnur et al. (13) reported that the most common medical disorders in the ICU in Houston were respiratory failure, disseminated intravascular coagulation, placental abnormalities, hemolysis elevated liver enzymes and low platelet count syndrome, chorioamnionitis, peripartum cardiomyopathy, puerperal sepsis, urinary infection, bacteremia, substance abuse, and asthma. In contrast, the ICU in Mumbai had higher incidence of neurologic disorders, renal and cardiovascular dysfunction, severe malaria, viral hepatitis, cerebral venous thrombosis, and poisoning Tables 5 and 6).

Prognostic Scoring. In general, obstetric patients admitted to the ICU tend to have lower mortality rates than general medical patients. Traditional prognostic scores such as APACHE II, APACHE III, and the Simplified Acute

Table 3. Organ involvement as defined by the Multiple Organ Dysfunction Score (MODS) in 928 obstetric patients admitted to the intensive care units of King Edward Memorial Hospital, Mumbai, India, and Ben Taub General Hospital, Houston, TX

	King Edward Memorial Hospital (n = 754)	Ben Taub General Hospital (n = 174)	Odds ratio (95% CI)
Organ dysfunction			
Neurological	477 (63.3%)	63 (36.2%)	3.03 (2.12–4.34)[b]
Cardiovascular	290 (38.5%)	50 (28.7%)	1.55 (1.07–2.26)[b]
Hepatic	274 (36.3%)	72 (41.4%)	0.81 (0.57–1.15)
Renal	373 (49.5%)	64 (36.8%)	1.68 (1.18–2.4)[b]
Hematological	420 (55.7%)	109 (62.6%)	0.75 (0.53–1.07)
Respiratory	345 (45.8%)	102 (58.6%)	0.66 (0.42–0.84)[b]
Disseminated intravascular coagulation[a]	172 (22.8%)	70 (40.2%)	0.44 (0.31–0.63)[b]
MODS scores			
MODS score on admission	4 (2–5) (range 0–12)	3 (2–5) (range 0–16)	—
Maximum MODS score	5 (3–7) range (0–16)	4 (2–6) range (0–22)	—[b]

[a]Disseminated intravascular coagulation is not a part of MODS; [b]difference was statistically significant ($p < .05$).
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Table 4. Medical and obstetric therapeutic interventions performed in 928 obstetric patients admitted to the ICUs of King Edward Memorial Hospital, Mumbai, India, and Ben Taub General Hospital, Houston, TX

	King Edward Memorial Hospital (n = 754)	Ben Taub General Hospital (n = 174)	Odds ratio (95% CI)
Medical interventions			
Mechanical ventilation	140 (18.6%)	100 (57.5%)	0.17 (0.12–0.24)[a]
Red cell transfusion	291 (38.6%)	90 (51.7%)	0.67 (0.48–0.95)[a]
Fresh frozen plasma	205 (27.2%)	61 (35.1%)	0.69 (0.48–0.99)[a]
Cryoprecipitate	32 (4.2%)	30 (17.2%)	0.21 (0.12–0.37)[a]
Platelets	89 (11.8%)	41 (23.6%)	0.44 (0.29–0.68)[a]
Inotropic drugs	160 (21.2%)	40 (23.0%)	0.9 (0.6–1.36)
Dialysis	62 (8.2%)	6 (3.5%)	2.51 (1.02–6.55)[a]
Obstetric interventions			
Cesarean section	116 (15.4%)	136 (78.2%)	0.05 (0.03–0.08)[a]
Hysterotomy	4 (0.5%)	8 (4.6%)	0.11 (0.02–0.42)[a]
Hysterectomy	32 (4.2%)	26 (14.9%)	0.25 (0.14–0.45)[a]
Curettage	43 (5.7%)	21 (12.1%)	0.44 (0.25–0.79)[a]
Induction of labor	201 (26.7%)	66 (37.9%)	0.1 (0.06–0.16)[a]

[a]Difference was statistically significant ($p < .05$).
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Physiology Score have not been accurate in predicting outcome in obstetric patients (6, 14–16). Several studies have tried to compare the APACHE II predicted mortality rate with the observed mortality rate. It was found that APACHE II score overestimated the maternal mortality rate (14–16). There are several reasons to explain those findings. The physiologic variables contained in the APACHE II score include variables that deviate from normal in the pregnant patient, thereby falsely elevating the score. These variables include maternal heart rate, respiratory rate, pH, and blood volume. Furthermore, the physiologic derangements that occur in critically ill pregnant patients usually resolve quickly, especially after the delivery of the fetus in several obstetric disorders, accounting for a lower mortality rate (18). Severity scores such as the APACHE II and Simplified Acute Physiology Score II may have a role in predicting mortality in obstetric patients admitted with medical disorders compared with obstetric illnesses (14, 17). The Sequential Organ Failure Assessment score might be a better predictor of mortality in this population as shown by the study by Karnad et al. (14). In patients with eclampsia, Glasgow Coma Scale score may be as good a predictor as APACHE II score.

Presenting Symptoms of Critical Illnesses in Pregnancy

In this section we review the common symptoms that pregnant patients can present with, and we discuss the differential diagnoses pertaining to each symptom. Most of the disorders covered in this section will be dealt with in more detail in the following sections of this supplement.

Shortness of Breath. Dyspnea is a common symptom in pregnancy. When a patient has shortness of breath, it is important to distinguish the dyspnea occurring due to underlying medical disorders vs. dyspnea secondary to normal physiologic changes that occur in pregnancy. Up to 70% of women experience the sensation of dyspnea during a normal and uncomplicated pregnancy (19, 20). The proposed mechanism is attributed to changes in cardiovascular and pulmonary physiology. The changes include an increase in blood volume resulting physiologic anemia, a decrease in functional residual capacity due to upward displacement of the diaphragm (21), and an increase in minute ventilation resulting in a respiratory alkalosis (22, 23).On the other hand, the obstetric patient presenting with an acute onset of shortness of breath deserves a careful evaluation to rule out diagnoses that can be life threatening for both the mother and the fetus. The most common disorders that can cause acute shortness of breath in an obstetric patient are listed in Table 7.

Cardiovascular diseases as a cause of dyspnea complicate 1–4% of pregnancies. Pregnant patients may have an underlying cardiac disease that may become

Table 5. Medical disorders requiring intensive care unit (ICU) admission in 928 obstetric patients admitted to the ICUs of King Edward Memorial Hospital, Mumbai, India, and Ben Taub General Hospital, Houston, TX

Medical disorders	King Edward Memorial Hospital (n = 754)	Ben Taub General Hospital (n = 174)	Odds ratio (95% CI)
Community-acquired pneumonia	23 (3.1%)	5 (2.9%)	1.06 (0.38–3.24)
Urinary tract infection	2 (0.3%)	18 (10.3%)	0.02 (0.00–0.10)[a]
Malaria	75 (10.0%)	0	38.8 (2.26–665)[a]
Hematological disorder	12 (1.6%)	1 (0.6%)	2.8 (0.38–58.0)
Congenital heart disease	2 (0.3%)	2 (1.2%)	0.23 (0.02–2.28)
Rheumatic heart disease	16 (2.1%)	2 (1.2%)	1.86 (0.41–11.9)
Aspiration pneumonia	23 (3.1%)	6 (3.5%)	0.88 (0.33–2.45)
Diabetes mellitus	16 (2.1%)	4 (2.3%)	0.92 (0.28–3.30)
Chronic renal failure	4 (0.5%)	1 (0.6%)	0.92 (0.10–21.8)
Trauma	0	1 (0.6%)	0.0 (0.0–3.8)
Drug abuse	0	5 (2.9%)	0.0 (0.0–0.26)[a]
Rheumatological disorders	2 (0.3%)	2 (1.2%)	0.23 (0.02–2.28)
Anaphylaxis	0	2 (1.2%)	0.0 (0.0–0.93)[a]
Asthma	1 (0.1%)	5 (2.9%)	0.04 (0.0–0.4)[a]
DVT/pulmonary embolism	5 (0.7%)	2 (1.2%)	0.57 (0.1–4.3)
Malignancy	1 (0.1%)	6 (3.5%)	0.4 (0.0–0.31)[a]
Acute abdomen	6 (0.8%)	10 (5.7%)	0.13 (0.04–0.40)[a]
CNS infection	6 (0.8%)	0	3.03 (0.16–57.3)
Viral hepatitis	47 (6.2%)	0	23.4 (1.36–404)[a]
Bacteremia	13 (1.7%)	8 (4.6%)	0.36 (0.14–0.98)[a]
Attempted suicide (poisoning/drug overdose)	13 (1.7%)	1 (0.6%)	3.0 (0.41–62.6)
Transfusion reaction	2 (0.3%)	1 (0.6%)	0.46 (0.03–12.9)
Cardiac arrest prior to ICU admission	21 (2.8%)	1 (0.6%)	4.96 (0.70–99.7)[a]
Endocrine	8 (1.1%)	1 (0.6%)	1.86 (0.23–39.8)
Arterial disease	1 (0.1%)	1 (0.6%)	0.23 (0.01–8.43)
Intracranial hemorrhage	9 (1.2%)	1 (0.6%)	2.09 (0.27–44.3)
Cerebral venous thrombosis	26 (3.5%)	0	12.7 (0.73–221)[a]
Tetanus	2 (0.3%)	0	1.16 (0.05–25.8)
Typhoid	1 (0.1%)	0	0.69 (0.02–18.3)
Leptospirosis	2 (0.3%)	0	1.16 (0.05–25.8)
Cerebral infarction	2 (0.3%)	0	1.16 (0.05–25.8)

[a]Difference was statistically significant ($p < .05$).
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Table 6. Obstetric conditions requiring intensive care unit (ICU) admission in 928 obstetric patients admitted to the ICUs of King Edward Memorial Hospital, Mumbai, India, and Ben Taub General Hospital, Houston, TX

Obstetric disorder	King Edward Memorial Hospital (n = 754)	Ben Taub General Hospital (n = 174)	Odds ratio (95% CI)
Pre-eclampsia/eclampsia	343 (45.5%)	74 (42.5%)	1.13 (0.80–1.6)
Postpartum hemorrhage	115 (15.3%)	32 (18.4%)	0.8 (0.51–1.26)
IUFD	94 (12.5%)	8 (4.6%)	2.96 (1.36–6.7)[a]
Post-abortal/puerperal sepsis	49 (6.5%)	26 (14.9%)	0.38 (0.22–0.66)[a]
HELLP syndrome	42 (5.6%)	31 (17.8%)	0.27 (0.16–0.46)[a]
Abruptio placentae	43 (5.7%)	15 (8.6%)	0.64 (0.34–1.24)
Acute fatty liver of pregnancy	33 (4.4%)	3 (1.7%)	2.61 (0.76–10.8)
Antepartum hemorrhage	27 (3.6%)	4 (2.3%)	1.58 (0.52–5.39)
Chorioamnionitis	7 (0.9%)	22 (12.6%)	0.06 (0.02–0.16)[a]
Abortions	18 (2.4%)	6 (3.5%)	0.68 (0.25–1.96)
Abnormal adherence of placenta	8 (1.1%)	9 (5.2%)	0.2 (0.07–0.56)[a]
Peripartum cardiomyopathy	4 (0.5%)	10 (5.8%)	0.09 (0.03–0.29)[a]
Uterine rupture	6 (0.8%)	3 (1.7%)	0.46 (0.1–2.33)
Amniotic fluid embolism	4 (0.5%)	1 (0.5%)	0.92 (0.1–21.8)

[a]Difference was statistically significant ($p < .05$).
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decompensated during pregnancy or may develop an occult illness that is associated with the pregnancy itself. Valvular heart diseases can be either congenital or acquired. Patients with valvular heart disease may decompensate due to the physiologic changes that occur during pregnancy and may develop pulmonary edema. The American Heart Association and the American College of Cardiology published guidelines for the management of pregnant patients with valvular heart disease (24). Peripartum cardiomyopathy is a rare dilated cardiomyopathy of unknown cause that occurs in the peripartum period. Peripartum cardiomyopathy is the fifth leading cause of maternal death. It can occur in the last month of pregnancy and up to 5 months after delivery (25). Peripartum cardiomyopathy is a rare disease; however, mortality can be as high as 20–50%.

Obstetric patients can present with shortness of breath due to embolic diseases. Venous air embolism can occur due to a variety of causes in the obstetric patient. It can occur during delivery, labor, abortions, placenta previa, orogenital sex, or central venous catheterization. The presenting symptoms typically are dyspnea, hypotension, tachycardia, tachy-

Table 7. Common causes of dyspnea in obstetric patients

Cardiovascular
Postpartum cardiomyopathy
Congenital heart disease
Valvular heart disease
Embolic disorders
Venous air embolism
Amniotic fluid embolism
Venous thromboembolism
Pulmonary
Pulmonary edema
Tocolytic induced pulmonary edema
Preeclampsia or eclampsia causing pulmonary edema
Ovarian hyperstimulation syndrome
Acute respiratory distress syndrome
Asthma exacerbation or status asthmaticus
Exacerbation of underlying pulmonary disorders
Aspiration syndrome (Mendelson's syndrome)
Pneumomediastinum and pneumothorax
Hematologic
Anemia
Physiologic (dilutional)
Acute blood loss
Infectious
Sepsis
Community-acquired pneumonia

pnea, or a sudden cardiac arrest. Physical exam may reveal the characteristic "Mill-wheel murmur." The mechanism underlying venous air embolism is thought to be due to air traveling through the placental venous sinuses into the venous circulation and thereafter into the right ventricle, causing obstruction of the right ventricular outflow tract. Treatment is usually supportive. The patient can be put in the left lateral decubitus position. Aspiration of air and hyperbaric oxygen has been tried with some success in few cases (26).

Venous thromboembolism is estimated to occur in 1–2 of 1,000 pregnancies (27). It can occur at any time during pregnancy but is more common in the prenatal period (28). Risk factors associated with increased risk for thromboembolism include prior history of deep vein thrombosis, use of oral contraceptive pills, presence of a hypercoagulable state, maternal age >30 yrs, obesity, and immobility.

Venous thromboembolism in pregnant patients is diagnosed similarly to nonpregnant patients. Diagnostic modalities such as ventilation perfusion scans and computed tomography angiography seem to be safe for use in pregnancy (29). Heparin is the mainstay of therapy in pregnant patients since it does not cross the placenta and can be stopped easily for the delivery. There is paucity of data regarding the treatment of unstable pulmonary embolism patients in regard to the use of thrombolytics and embolectomy.

Amniotic fluid embolism is a rare disorder occurring in 1 of 8,000 to 1 of 80,000 deliveries. The most common presenting symptoms are hypotension, fetal distress, pulmonary edema or acute respiratory distress syndrome, and cardiopulmonary arrest. There is no known diagnostic test that can confirm the diagnosis. The diagnosis is usually based on the constellation of clinical symptoms and signs. Treatment is usually supportive (30).

A variety of pulmonary disorders that occur in pregnancy can present with dyspnea. Pulmonary edema can be cardiogenic and noncardiogenic in origin. Cardiogenic causes have been discussed earlier in this article. Noncardiogenic pulmonary edema or acute respiratory distress syndrome can occur following a variety of insults, including the use of tocolytics, aspiration of gastric content, preeclampsia or eclampsia, sepsis, trauma, and following the transfusion of multiple blood products (31). Tocolytic induced pulmonary edema is a unique disorder of pregnancy. It is the underlying cause in about 25% of cases of pulmonary edema (32). It occurs following the use of β-sympathomimetic agents like ritodrine and terbutaline. The underlying mechanism is not well understood; however, it is thought to be due to several factors including increased heart rate, elevated cardiac output, myocardial dysfunction due to prolonged use of catecholamines, and increased capillary permeability. Treatment consists of cessation of tocolytic therapy, diuresis, and oxygen therapy (31). Most patients respond, and mortality is very rare (33).

Mendelson (34) in 1946 described 66 cases of pulmonary aspiration of gastric content in 44,016 pregnancies (which later came to be referred as "Mendelson syndrome"). He noted two fatalities. Gastric content aspiration occurs in pregnant patients due to a relaxed gastroesophageal sphincter, elevated intragastric pressure, decreased gastric motility, and diminished gastric emptying during parturition (31). Diagnosis is usually by clinical suspicion as well as radiographic findings. Treatment is usually supportive.

Ovarian hyperstimulation syndrome (OHSS) is another condition that can present with pulmonary edema due to increased vascular permeability. OHSS is a complication that occurs due to administration of exogenous gonadotropins and clomiphene citrate to induce ovulation in *in vitro* fertilization. The prevalence of OHSS ranges between 1% and 10% (35). Risk factors associated with the occurrence of OHSS include age <35 yrs, low body mass index, presence of polycystic ovary syndrome, high serum estradiol levels, multiple follicles, necklace sign on ultrasonography, and pregnancy (36). OHSS is classified as mild, moderate, severe, and life threatening. Life-threatening OHSS is characterized by a variably enlarged ovary, tense ascites with or without hydrothorax, hematocrit >55%, white blood cell count >25,000, oliguria, creatinine level ≥1.6 mg/dL, creatinine clearance <50 mL/min, renal failure, thromboembolic phenomena, and acute respiratory distress syndrome (37, 38). Management is usually supportive and includes prevention of possible complications.

Other conditions that may present during pregnancy include the exacerbation of underlying pulmonary disorders including asthma. Both topics are reviewed in detail in this supplement.

Other causes such as asthma and pneumonia are reviewed elsewhere in this issue.

Jaundice. Jaundice is a common presenting symptom in pregnancy, occurring in about 20% of obstetric patients admitted to the ICU (13). A variety of conditions can present with jaundice; some are unique to pregnancy, whereas others are not. The most common causes of jaundice in pregnancy are listed in Table 8.Disorders that are unique to pregnancy include fatty liver of pregnancy, hemolysis elevated liver enzymes and low platelet count syndrome, severe preeclampsia or eclampsia, intrahepatic cholestasis of pregnancy, and hyperemesis gravidarum. Most of those disorders are covered in the section on liver disease. Hyperemesis gravidarum is associated with hyperbilirubinemia and elevated serum aminotransferases in about 50% of patients admitted to the hospital (39). Alanine aminotransferase is usually higher than aspartate aminotransferase; however, the magnitude of elevation is usually mild (40). The degree of liver abnormalities usually correlates with the degree of vomiting. In the presence of the typical clinical scenario, there is no need for a liver biopsy for diagnosis. Liver abnormalities resolve once hyperemesis abates (40–42).

Acute viral hepatitis is a common dis-

Table 8. List of causes of jaundice in the obstetric patient

Intrahepatic cholestasis
Fatty liver of pregnancy
Viral hepatitis
Hepatitis B
Hepatitis C
Hepatitis E
HELLP syndrome
Eclampsia
Intrahepatic cholestasis of pregnancy
Ruptured liver hematoma
Wilson's disease
Sepsis
Toxic ingestion
Hyperemesis gravidarum
Congenital disorders
Crigler-Najjar type II
Ovarian hyperstimulation syndrome
Extrahepatic cholestasis
Acute cholecystitis
Budd-Chiari syndrome
Hemolytic disorders
Malaria
HELLP syndrome
HUS-TTP
DIC

HELLP, hemolysis, elevated liver enzymesh and low platelets; HUS, hemolytic uremic syndrome; TTP, thrombotic thrombocytopenic purpura; DIC, disseminated intravascular coagulation.

Table 9. Causes of fever in the pregnant patient

Obstetric
Intra-amniotic infection
Chorioamnionitis
Premature rupture of membranes
Amnionitis
Postpartum endometritis
Septic abortion
Episiotomy infection
Cellulitis
Necrotizing fasciitis
Myonecrosis
Septic pelvic thrombophlebitis
Mastitis
Nonobstetric
Urinary tract infections
Uncomplicated urinary tract infection
Pylonephritis
Pneumonia
Community-acquired pneumonia
Bacterial
Viral (varicella, influenza, SARS)
Fungal
Hospital-acquired pneumonia
Aspiration pneumonia
Intra-abdominal infections
Appendicitis
Cholecystitis
Viral hepatitis (A, B, C, D, E)
Human immunodeficiency virus
Malaria
Lyme disease
Disseminated herpes infections
Listeriosis
Sexually transmitted diseases

SARS, severe acute respiratory syndrome.

ease that may be acquired in pregnancy. Hepatitis may be the admitting diagnosis in up to 6.2% of patients presenting to the ICU (13). This usually occurs more frequently in developing countries. Hepatitis B and C infections in pregnancy are covered in detail in the section on liver diseases. Acute hepatitis E usually causes epidemic and sporadic acute self-limiting hepatitis in endemic areas. In a retrospective study from New Delhi, India, 62 pregnant women presenting with jaundice in the third trimester were analyzed. Hepatitis E infection was present in 45% of the patients. Of the women with hepatitis E virus infection, 82% had fulminant hepatic failure. Mortality rate was very high (26.9%). In the non-hepatitis E virus group, mortality rate was lower. Vertical transmission occurred in 33.3% of the cases (43).

Malaria is another infection that presents with jaundice. Prevention of malaria in pregnancy is important because the disease can cause significant maternal and fetal complications. Pregnant women have a higher risk of acquiring malaria (44). Malaria accounts for 10% of patients requiring ICU admission in developing countries (13, 14). The prevalence of malaria decreases with increasing parity. Malaria infection is more common in primigravidae (45). The placenta appears to be the site of multiplication of the parasite. The usual presenting symptoms are chills, sweats, headache, myalgias, fatigue, nausea, abdominal pain, vomiting, diarrhea, jaundice, and cough. However, in some cases the disease can be more severe, causing severe hypoglycemia and respiratory failure secondary to acute respiratory distress syndrome (46). It is also associated with low birth weight infants. Chemoprophylaxis is essential in endemic areas.

Crigler-Najjar type II disease is a rare cause of maternal unconjugated hyperbilirubinemia in pregnancy. Crigler-Najjar disease is of two types. Type I is fatal. Patients with type II can survive to adulthood without neurologic sequelae. The disease is characterized by a genetic defect in the enzymes responsible for bilirubin conjugation (47). Type II disease usually causes mild elevations in bilirubin. The bilirubin can be transferred to the fetus; however, the jaundice resolves without apparent sequelae (48).

Fever. Fever is one of the most common presenting manifestations in pregnant patients admitted to the ICU; fever can be present in up to 55% of patients (13). Numerous diseases can cause fever in the pregnant patient. They can be subdivided into obstetric disorders, in which the disorder is unique to this patient population and involves an infection that is related to the pregnancy itself, and nonobstetric disorders, which are general medical disorders that either can manifest in pregnancy due to increased susceptibility or can lead to complications in both the fetus and the mother. A list of possible causes of fever in a pregnant patient presenting to the ICU is shown in Table 9.

Obstetric-related infections comprise the majority of the disorders presenting with fever to the ICU in a pregnant patient (13). Intra-amniotic infections include a spectrum of diseases such as chorioamnionitis, amnionitis, and amniotic fluid infection. Intra-amniotic infections can complicate up to 10% of deliveries (49). The infection often is due to more than one microbial pathogen. Diagnosis is made in pregnant patients with fever if at least two of the following criteria are present: maternal leukocytosis, maternal tachycardia, fetal tachycardia, uterine tenderness, and foul-smelling amniotic fluid (50). Diagnosis can be confirmed by culture, amniotic fluid Gram stain, white cell count, glucose, and cytokine levels. Sepsis complicates intra-amniotic infections in only 0.5–1.3% of cases (51, 52). Antibiotics reduce maternal and fetal morbidity. Timing of delivery does not affect outcome (51).

Postpartum endometritis is caused by infection of the decidua with possible extension to the myometrium and parametrial tissues. It is more common in patients undergoing cesarean section. Diagnosis is made on clinical criteria that include fever, uterine tenderness, foul smelling discharge, and leukocytosis within 5 days of delivery (53). Endometritis is usually a polymicrobial infection in up to 70% of the cases (54). Treatment is with broad-spectrum antibiotics that can cover anaerobes. Septic abortion is an infection following termination of pregnancy, which can be either spontaneous or induced. The risk of infection following an induced abortion is about 1%. Infections can range from a localized endometritis, extension to the parametrial tissues, formation of a pelvic abscess to the systemic sepsis. The microbial pathogens are primarily derived from the vaginal bacterial flora but can result from sexually transmitted organisms such as

Chlamydia trachomatis or *Neisseria gonorrhea*. Reevacuation of the uterus and antibiotics are the mainstay of therapy (55).

Septic pelvic thrombophlebitis can complicate pelvic procedures and is thought to be preceded by a pelvic infection. It was first described by Collins et al. (56) in 1951, when he reported on 70 cases. Patients present with an unexplained fever that is unresponsive to antibiotics. Diagnosis is made clinically and may be confirmed by CT scan. Treatment is usually with antibiotics and heparin. Surgery is rarely needed (57).

Episiotomy, which consists of the perineal surgical incision at the time of parturition can be complicated by infection, dehiscence, fistula formation, sepsis, and necrotizing fasciitis and myonecrosis. Uncomplicated infection manifest with fever, swelling, pain and tenderness, and purulent discharge. Drainage and debridement are indicated in addition to systemic antibiotics. Necrotizing fasciitis is a more severe infection, often polymicrobial; however, it can result from clostridial organisms. Antibiotic treatment usually includes a penicillin and clindamycin. Extensive surgical debridement until healthy bleeding tissue is encountered is the mainstay of therapy. Necrotizing fasciitis carries a high mortality rate of up to 50% (58).

Nonobstetrical infections are less common in pregnancy but, nonetheless, carry a high morbidity to the pregnant patient and may result in admission to the intensive care unit. In a study comparing a medical ICU in Houston, Texas, with a similar ICU in Mumbai, India, community-acquired pneumonia, urinary tract infection, and bacteremia were more common in the U.S. ICU. Malaria, central nervous system infection, and viral hepatitis were the most common nonobstetrical infections in India (18). Malaria and viral hepatitis were previously discussed in the section on jaundice. Sepsis will be covered extensively in a separate manuscript in the supplement. Pneumonia in pregnant patients is occasionally associated with significant maternal and fetal morbidity including respiratory failure, prolonged hospitalization, and low birth weight at delivery. The most common form of pneumonia is community-acquired (pneumococcal) pneumonia; however, viral and fungal pneumonia can occur. Pregnant patients may be more susceptible to such infections due to a decrease in cell-mediated immunity. A detailed review of pneumonia in pregnancy is presented in this supplement.

Urinary tract infections can range from asymptomatic bacteriuria to cystitis and acute pylonephritis. Acute pylonephritis can complicate 14 of 1,000 deliveries (59). Pylonephritis was associated with nulliparity and young age. It occurs more often in the second trimester. The predominant organism is *Escherichia coli*. Complications can include anemia, sepsis, renal dysfunction, and respiratory failure (59). Pregnant patients are predisposed to pylonephritis due to the pregnancy-related changes in urinary tract anatomy. These changes include pressure on the bladder from the enlarging uterus and an increase in the size of the ureters due to smooth-muscle relaxation. The risk of preterm birth is not increased in patients with pylonephritis (59).

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