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Abstract

Morbidity and mortality associated with sepsis has gained widespread attention on a local, state, and national level, yet, it remains a complicated disorder that can be difficult to identify in a timely manner. Sepsis in obstetric patients further complicates the diagnosis as alterations in physiology related to pregnancy can mask sepsis indicators normally seen in the general population. If early signs of sepsis go unrecognized, septic shock can develop, leading to organ dysfunction and potential death. Maternal early warning tools have been designed to assist clinicians in recognizing early indications of illness. Through use of clinical pathway-specific tools, disease processes may be detected early, subsequently benefitting patients with aggressive treatment management and intervention.

This article is the second in a series of three that discuss the importance of sepsis and septic shock in pregnancy. Risk factors, causes of sepsis, signs and symptoms, and maternal early warning tools are discussed.

Key words: Obstetrics; Risk factor; Screening; Sepsis.

Sepsis in Obstetrics
CLINICAL FEATURES and
EARLY WARNING TOOLS

Sheryl E. Parfitt, MSN, RNC-OB, Mary L. Bogat, MSN, RNC-OB, Sandra L. Hering, MSN, RNC-OB, CPHIMS, Charlotte Ottley, MSN, RNC-OB, and Cheryl Roth, PhD, WHNP-BC, RNC-OB, RNFA

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Carol Decker looked forward to the arrival of her second child; another little girl. At 31 weeks gestation, her pregnancy had been problem free. But one morning she awoke and noticed a sharp pain in her left side. Thinking she may be experiencing a kidney stone, she went to the local emergency room where an on-call obstetrician did not find anything wrong. She was discharged home. The pain did not subside so Carol drove to her obstetrician's office, about an hour away. He admitted her to the hospital for an overnight stay, but again, she was sent home and told that nothing was wrong. The next day, Carol began aching all over. Within 8 days, she spiked a temperature of 38.9 ºC/ 102 ºF. She called her obstetrician and was instructed to take some acetaminophen. In spite of taking the medication, Carol's fever continued to rise until it was 39.5 ºC/103 ºF. She also began experiencing uncontrolled pain throughout her entire body, as well as uterine contractions. By the time she and her husband reached the hospital at which her obstetrician delivered, she was doubled over with pain and was experiencing diarrhea. On admission, fetal status appeared to be compromised, so an emergency cesarean birth was performed. What no one knew or understood at that time was that Carol was septic from a streptococcal infection. When she finally awoke 20 days later, her world was very different. Although she survived the massive infection and resultant septic shock, Carol lost the ring finger on her right hand, her left arm below the elbow, both feet, a large portion of her skin, as well as her eyesight.

Overview

Maternal infections are common due to physiologic changes of pregnancy (Morgan & Roberts, 2013). Invasion of microorganisms normally found in the genitourinary tract can lead to development of frequent urinary tract infections, pyelonephritis, and what has been known as chorioamnionitis in the past (Higgins et al., 2016; Morgan & Roberts). An expert panel convened in January 2015 by the Eunice Kennedy Shriver National Institute of Child Health and Human Development recommended using intrauterine inflammation or infection or both, abbreviated as Triple I, instead of chorioamnionitis (Higgins et al.). Sepsis is characterized by an overexaggerated, systemic inflammatory response to an invasive organism. If this response is not recognized and treated in a timely manner, septic shock can develop, leading to severe hypotension, inadequate perfusion, widespread injury at the cellular level, ischemia, organ dysfunction, and potential death. Fortunately, most obstetric patients are young and healthy so they easily fight any acquired infection before it can progress to sepsis and septic shock (Morgan & Roberts). The purpose of this article is to discuss risk factors, causes, and signs and symptoms associated with maternal sepsis and to review maternal early warning tools that can be helpful in early detection of deteriorating vital signs and laboratory values associated with sepsis.

> Identification of signs and symptoms associated with development of sepsis in obstetric patients remains a problematic issue.

Risk Factors

Risk factors correlated with development of sepsis during pregnancy are obesity, poor nutrition, chronic hypertension, diabetes mellitus, anemia, decreased function of the spleen, immunosuppression, invasive procedures, and history of group B streptococcal infection. Additional factors include lack of prenatal care, nonwhite ethnicity, poverty, first pregnancies, and use of antibiotics within 2 weeks of birth, including prophylaxis for cesarean sections (Chebbo, Tan, Kassis, Tamura, & Carlson, 2016).

During the intrapartum period, women experiencing prolonged rupture of membranes, lengthened active labor phase, more than five vaginal examinations during the second stage of labor, or operative vaginal birth have a higher incidence of sepsis. According to Chebbo et al. (2016), the single most important risk factor for sepsis during the birth process is an unscheduled cesarean, contributing to a 5- to 20-fold greater risk of infection than a vaginal birth. Mothers who develop cracked nipples, mastitis, or experience problems associated with retained placental fragments during postpartum have the potential of developing sepsis (Chebbo et al.; Morgan & Roberts, 2013).

Causes

Changes in maternal immune responses occur during pregnancy to protect the unborn fetus from rejection. There is an overall downregulation of the inflammatory response leading to decreased T-cell activity, cell-mediated immunity, and release of cytokines. These changes may predispose pregnant patients to development of infections from fungi, viruses, and bacteria that would typically not cause a problem (Chebbo et al., 2016).

Morgan and Roberts (2013) reported four infectious conditions associated with pregnancy that may lead to development of sepsis: (1) pyelonephritis; (2) chorioamnionitis; (3) septic abortion; and (4) pneumonia. In the United States, 3% to 4% of all antepartum admissions are due to pyelonephritis (Morgan & Roberts). The influence of progesterone leads to dilation of the ureters, and as the pregnant uterus enlarges, it compresses the urinary system leading to blockage, stasis, and bacterial growth. Although rare, development of septic shock during pregnancy is most often caused by pyelonephritis. Women may present with fever, vomiting, decreased appetite, and hypovolemia (Morgan & Roberts). It is important to be able to distinguish between transient hypotension that responds to intravenous fluids and signs of septic shock, which include persistent hypotension and decreased perfusion to vital organs in spite of adequate fluid resuscitation (Morgan & Roberts).

Intrauterine inflammation or infection or both (Triple I) is characterized by acute inflammation and/or infection

of the chorion, amnion, and placenta (Higgins et al., 2016). It can occur with or without rupture of membranes and is seen in approximately 1% to 4% of all term births and 5% to 10% of preterm births (Morgan & Roberts, 2013). Cases of septic abortion are rarely seen at this time in the United States and mortality rates associated with both bacterial and viral pneumonias have significantly decreased with improved treatment plans (Morgan & Roberts).

Postpartum endometritis is a fairly common type of infection involving the lining of the endometrium, myometrium, and parametrium that can lead to necrotizing fasciitis and sepsis. It is usually caused by both anaerobic and aerobic polymicrobial pathogens including *Peptostreptococcus*, *Clostridium* spp., Group B *streptococcus*, *enterococcus*, and *Escherichia coli*. These organisms ascend from the lower genital tract during labor. Patients presenting with hematomas or extensive tissue damage following birth are at a higher risk for sepsis secondary to bacterial growth and infection (Morgan & Roberts, 2013).

Gram-negative and gram-positive organisms are the most common causes of septic shock, producing endotoxins and exotoxins that generate a heightened inflammatory response leading to increased endothelial dysfunction and vascular permeability (Kaponis, Filindris, & Decavals, 2012). Group A Streptococcus pyogenes (GAS) is a virulent, potentially lethal organism causing abdominal pain, fever, and tachycardia. Although this condition can be present at any time during pregnancy, as in Carol Decker's case, postpartum women are at a 20-fold increased risk for developing GAS compared to the nonobstetric population. Exotoxins produced by this organism can cause widespread tissue necrosis of major organs including the kidneys, leading to toxic shock syndrome and the potential of a 60% mortality rate (Chebbo et al., 2016).

Signs and Symptoms

Identification of signs and symptoms associated with development of sepsis in obstetric patients remains a problematic issue. Physiologic changes related to pregnancy such as increased fluid volumes that lead to an intensified demand on cardiac and renal systems, respiratory adaptations, and deviations in metabolic demands can mask sepsis indicators normally seen in the general population (Casey, Hayes, & Ross, 2013). Symptoms can vary from person to person. Women may present with flu-like symptoms such as a fever, upper respiratory infection, or nausea and vomiting (Barton & Sibai, 2012). Carol Decker's initial presenting symptoms did not present as a potentially infectious process, but even after she reported body aches and a fever, sepsis was not suspected. Lack of sepsis recognition, delay in antibiotic treatment, and deficiencies in escalation of care are three major contributors to poor outcomes associated with sepsis (Bauer, Lorenz, Bauer, Rao, & Anderson, 2015).

Clinical characteristics that consistently appear to be present in maternal sepsis cases include pyrexia (>38 °C) or hypothermia (<36 °C), persistent tachycardia (>110/min), tachypnea (>24), and abnormally low or elevated white blood cell (WBC) counts (Casey et al., 2013; Shields, Wiesner, Klein, Pelletreau, & Hedriana, 2016). White blood cell counts of pregnant women are normally elevated, especially at birth, making WBC use as an indicator for infection more challenging. An increase in maternal temperature, generally considered to be ≥38 °C, is also commonly seen

Early warning criteria for the nonobstetric adult population do not take into consideration the physiologic changes of pregnancy.

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in labor, further complicating a timely diagnosis (Chen, 2016; Sivasankar, Kumar, Baraz, & Collis, 2015). Clotting abnormalities are almost always present in patients experiencing sepsis and may range from slight changes in laboratory values to widespread disseminated intravascular coagulation from the abnormal inflammatory response (Pacheco, Saade, & Hankins, 2014).

The presence of vomiting and diarrhea, abdominal pain that is disproportionate for the presenting problem, and indeterminate or abnormal fetal heart rate patterns, particularly tachycardia, are conditions that warrant further observation and testing. Sepsis can also be portrayed by alterations in mental function due to impaired perfusion, dysfunction of the blood-brain barrier, persistent hyperglycemia, and prolonged inflammation (Casey et al., 2013; Sonneville et al., 2013). Women may appear confused, distracted, or disoriented with fluctuating levels of consciousness. Treatment should focus on reducing the inflammatory process and duration of the brain insult (Sonneville et al.).

Standardized Early Warning Tools

Use of standardized early warning tools to improve quality and patient safety has been shown to assist clinicians in quickly identifying and treating conditions that may lead to patient morbidity and mortality. Other benefits of these tools include decreased litigation and expenditures related to adverse patient outcomes, as well as improved reimbursements (Arora et al., 2016).

There are a number of early warning tools available for the nonobstetric adult population, such as the APACHE II (Knaus, Draper, Wagner, & Zimmerman, 1985), Modified Early Warning System (MEWS) (Mhyre et al., 2014), and Sequential Organ Failure Assessment (SOFA) score (Abraham, 2016), which assist in predicting patient outcomes related to sepsis and other critical illnesses. Even though sensitivity of these tools is generally within an acceptable rate, positive predictive values associated with intensive care unit (ICU) admissions and death are almost always low, which has led to revisions of existing criteria (Antonelli et al., 2016; Singh, McGlennan, England, & Simons, 2012). Early warning criteria for the nonobstetric adult population do not take into consideration the physiologic changes of pregnancy. Use of the nonobstetric warning criteria may lead to an overdiagnosis of sepsis in the obstetric population, desensitizing clinicians to triggers for truly septic patients (Albright, Ali, Lopes, Rouse, & Anderson, 2014). This issue has brought about development of several Modified Obstetric Early Warning Scoring (MOEWS) systems (Edwards et al., 2015).

A retrospective cohort study compared six MOEWS systems to determine if they correctly identified severe sepsis in women with a diagnosis of chorioamnionitis (Edwards et al., 2015). Results demonstrated that MOEWS scales currently in use vary widely in their alert criteria and accuracy. The majority of these six tools were shown to be poor predictors of sepsis in the obstetric population by overdiagnosing the condition. The authors stated that further research using MOEWS in the obstetrical setting is needed (Edwards et al.). Maguire and Turner (2015) highlighted that this study started with a total of 913 women, with 549 having to be excluded, based upon incomplete documentation of vital signs. They view MOEWS potential benefit to be an improvement in the recording of vital signs rather than a predictor of sepsis (Maguire & Turner). This has been demonstrated in Ireland with the introduction of the Irish Maternity Early Warning System, a nationally accepted standardized MOEWS used for all pregnant and postpartum patients in Ireland. It was first implemented in 2013 and has demonstrated an improvement in documentation of vital signs, particularly respiratory rate, in women diagnosed with maternal bacteremia (Maguire et al., 2015).

The 2003–2005 Confidential Enquiry into Maternal and Child Health (CEMACH) developed and implemented the Modified Early Obstetric Warning System (MEOWS) that is widely used throughout Great Britain for auditing maternal safety standards within the National Health Systems (Mhyre et al., 2014). It consists of trigger thresholds for temperature, blood pressure, heart rate, respiratory rate, oxygen saturation, pain score, and neurologic response. Patient results fall into either a Yellow trigger zone or a Red trigger zone depending on the severity of their symptoms. Researchers using data from a large tertiary referral center found that this tool's overall performance metrics demonstrated a higher sensitivity for patient morbidity than use of a nonobstetric adult population warning systems that measured death or ICU admissions (Singh et al., 2012). Limitations of the MEOWS tool included no universal definition for obstetric morbidity or validity of the criteria and inconsistent use due to increased documentation, decreased clinician compliance, and high numbers of false alarms (Mhyre et al.; Singh et al.).

> Through the use of clinical pathway-specific tools, disease processes may be detected early, subsequently benefitting patients with aggressive treatment management and intervention.

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The Maternal Early Warning Trigger (MEWT) tool was presented at the 36th Annual Meeting of the Society for Maternal-Fetal Medicine in February 2016, and was published in April 2016 (Shields et al., 2016). This tool examines four main causes of maternal morbidity and serves as a guide for clinicians in prompt evaluation and treatment of patients who present with potential sepsis, cardiopulmonary disorders, hypertension, and hemorrhage. There are two levels used to activate the tool: nonsevere triggers and severe/single abnormal triggers. Initiation of nonsevere triggers requires at least two abnormal values that persist for 20 minutes or more when assessing maternal temperature, blood pressure, heart rate, respiratory rate, oxygen saturation, altered mental status, or pain that is out of proportion for the presenting condition (Table 1). The sepsis pathway includes a fetal heart rate greater than 160 as an additional trigger point. Severe/single abnormal triggers require only one abnormal point to initiate use of the tool and include maternal heart rate, mean arterial pressure, respiratory rate, oxygen saturation, as well as nurses' perception that the patient is clinically unstable (Table 2). Once triggers are noted or if a nurse is clinically uncomfortable with the patient's presentation, the physician is notified for additional testing and treatment (Shields et al.).

A project implemented in 6 of 29 hospitals in a large hospital network evaluated use of the MEWT tool (Shields et al., 2016). Outcome measures for severe and composite maternal morbidity from the Centers for Disease Control and Prevention as well as ICU admissions were assessed. Researchers concluded that use of the MEWT tool demonstrated notable improvement in maternal morbidity and composite maternal morbidity. The tool was studied in varied hospital settings potentially making it applicable to most obstetrical units in the United States (Shields et al.).

Lack of Maternal Early Warning Tool and Recognition of Development of Sepsis: Implications for Carol Decker
In Carol Decker's case, no maternal early warning tool was available to alert clinicians that she was experiencing effects of sepsis. Bacteria stealthily grew unnoticed and by the time the seriousness of her condition was recognized, she was already suffering effects of a dysfunctioning inflammatory process causing vasodilation, destruction of the endothelial lining of her vessels, fluid leaks into extravascular spaces, and severe hypotension. The resultant septic shock, along with vasopressors used to support her blood pressure, caused vasoconstriction of blood vessels throughout her system leading to a profound lack of oxygen to tissues and organs. Her skin bubbled and sloughed off, organs began to fail, and blood circulation to her extremities was effectively cut off. In the end, Carol lost her right middle finger because staff did not remove a favorite ring as she began to become edematous. She lost her eyesight and extremities due to a lack of oxygen, all because her initial condition went unrecognized.

Clinical Implications
The importance of recognizing infectious processes that may lead to sepsis in obstetric patients cannot be overemphasized. Signs and symptoms of sepsis noted in the general population may be attributed to normal physiologic

TABLE 1. Maternal Early Warning Trigger Tool Nonsevere Trigger Points

Maternal temperature	>38 °C or <36 °C
Systolic blood pressure	<85 mmHg
Diastolic blood pressure	<45 mmHg
Maternal heart rate	>110 or <50 beats/min
Respiratory rate	>24 or <10/min
Oxygen saturation	<93%
Fetal heart rate (sepsis pathway only)	>160
Altered mental status	
Disproportionate pain	

Note: Two abnormal values sustained for >20 minutes used to trigger use of the tool. Used with permission from Shields et al. (2016).

TABLE 2. Maternal Early Warning Trigger Tool Severe or Single Abnormal Triggers

Heart rate	>130 beats/min
Respirator rate	>30/min
MAP	<55 mmHg
Oxygen saturation	<90%
Nurse clinically uncomfortable with patient's status	

Note: One abnormal value triggers use of the tool. Used with permission from Shields et al. (2016).

changes of pregnancy masking an underlying infection. Without prompt treatment, sepsis has the potential of becoming a stealthy, deadly killer as patients succumb to septic shock and end-organ dysfunction.

Nurses may be the first clinician a patient sees; therefore, their clinical judgment in determining patient status is critical in early identification of potential health issues. Use of an early warning tool designed for the obstetric population can assist clinicians in identifying important changes in patient vital signs, fetal heart rate patterns, laboratory values, and alterations in mental status (Shields et al., 2016). Protocols from the tool can then be activated to alert providers and rapid response teams of potential patient deterioration. When choosing a suitable tool, clinical teams must ensure ease of use, identification of triggers signifying clinical deterioration of the patient, and clear management guidelines that assist in better patient outcomes (Shields et al.). As shown in the retrospective cohort study that compared six MOEWS systems (Edwards et al., 2015), tools that do not fit these criteria result in incomplete data and have the potential of not being used. Adoption of an early warning tool that provides protocols and checklists can assist in providing optimal care to obstetric patients resulting in increased patient safety and improved outcomes (Arora et al., 2016).

Suggested Clinical Nursing Implications

- Physiologic changes related to pregnancy can mask sepsis indicators normally seen in the general population (Shields et al., 2016).

- Nurses can identify risk factors for sepsis that may include poor nutrition, chronic hypertension, diabetes mellitus, anemia, lack of prenatal care, poverty, first pregnancies, use of antibiotics within 2 weeks of birth, prolonged rupture of membranes, lengthened active labor phase, more than five vaginal examinations during the second stage of labor, operative vaginal birth, unscheduled cesareans, cracked nipples, mastitis, and retained products of conception (Chebbo et al., 2016).

- Clinical characteristics of sepsis that should be recognized and reported include pyrexia or hypothermia, tachycardia, tachypnea, abnormally low or elevated WBC, vomiting and diarrhea, abdominal pain that is disproportionate for the patient's presenting problem, fetal heart rate patterns that are associated with maternal infection such as tachycardia, and alterations in mental function (Chen, 2016; Sivasankar et al., 2015).

- Use of maternal early warning trigger tools may lead to prompt evaluation and treatment of septic obstetric patients (Shields et al., 2016).

best patient outcomes. Carol states that every day she is thankful to be alive and that she has the ability to be there for her husband and two daughters. For more information on Carol Decker see www.caroljdecker.com. ✤

Sheryl E. Parfitt is a Clinical Educator, HonorHealth Scottsdale Shea Medical Center, Scottsdale, AZ. The author can be reached via e-mail at sheryl.parfitt@honorhealth.com

Mary L. Bogat is a Staff Nurse, HonorHealth Scottsdale Shea Medical Center, Scottsdale; Clinical Instructor, Scottsdale Community College, Scottsdale and Arizona State University, Tempe, AZ.

Sandra L. Hering is Informatics Support Specialist, HonorHealth Scottsdale Shea Medical Center, Scottsdale, AZ.

Charlotte Ottley is Clinical Director, HonorHealth Scottsdale Osborn Medical Center, Scottsdale, AZ.

Cheryl Roth is a Nurse Practitioner, HonorHealth Scottsdale Shea Medical Center, Scottsdale, AZ.

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