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Sepsis and Septic Shock in Pregnancy

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Abstract

Sepsis during pregnancy is a critical condition that leads to organ dysfunction due to an abnormal response to infection. It remains a significant cause of maternal morbidity and mortality worldwide. The World Health Organization (WHO) reports a global prevalence of 4.4% of live births affected by maternal sepsis, with varying incidences across countries. Sepsis ranks among the top five causes of maternal deaths globally, contributing to 12.7% of pregnancy-related mortality in the United States. The physiological changes during pregnancy, such as increased blood volume and immune response modulation, create conditions that make pregnant individuals more susceptible to infections, complicating the timely diagnosis of sepsis. Due to these physiological differences, common sepsis screening tools like qSOFA and SOFA are often inadequate in pregnant patients, highlighting the need for specialized diagnostic and management strategies. Early detection and timely treatment are essential to improving maternal outcomes. Several screening tools, such as the Maternal Early Warning Trigger (MEWT) tool, have been designed to aid in the early identification of deteriorating maternal health. Once sepsis is suspected, prompt antibiotic therapy, fluid resuscitation, and vasopressor support are critical to prevent progression to septic shock. Additionally, controlling the infection source through surgical intervention or drainage may be necessary. Despite advances in sepsis management, challenges remain, particularly in identifying and treating sepsis in pregnant patients due to overlapping symptoms with normal pregnancy changes. Therefore, early recognition and appropriate intervention are key to reducing the impact of sepsis during pregnancy.

Introduction

Sepsis is a major cause of maternal illness and death, with a global prevalence of 4.4% among live births. It is the second leading cause of pregnancy-related mortality, responsible for 12.7% of maternal deaths (Evans et al., 2021; Khan et al., 2017; Kim et al., 2018; Sikora & Zahra, 2023). Septic shock is a severe form of sepsis, characterized by the need for vasopressors to maintain a Mean Arterial Pressure (MAP) of 65 mmHg and serum lactate levels above 2 mmol/L (>18 mg/dL) without hypovolemia. Although rare in pregnancy, occurring in 0.002% to 0.01% of deliveries, it has a mortality rate exceeding 40% (Khan et al., 2017; Sikora & Zahra, 2023).

Pregnancy-related physiological changes increase susceptibility to sepsis and can obscure typical symptoms, complicating diagnosis. Early detection is crucial due to the preventable

nature of sepsis and its impact on maternal health. Several screening tools are available to aid diagnosis, including the Quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA), Systemic Inflammatory Response Syndrome (SIRS), the modified obstetric early warning scoring system (MOEWS), and the Sepsis in Obstetrics Score (SOS) (Bauer et al., 2019; Bridwell et al., 2019; Fan et al., 2020; Greer et al., 2020; Parfitt et al., 2017; Parfitt & Hering, 2018). The diagnostic criteria for sepsis outlined by the Surviving Sepsis Campaign (SSC) are not suited for obstetric patients; however, the SSC treatment bundles remain useful as a reference for managing sepsis in obstetric cases (Bauer et al., 2019; Evans et al., 2021).

Early identification, diagnosis, and treatment of maternal sepsis are crucial for better outcomes. Reviews show that 63% of maternal deaths from sepsis were linked to inadequate care, often due to delays in recognizing the condition, especially in obstetric units. This leads to preventable morbidity and treatment delays (Fan et al., 2020; Greer et al., 2020). This paper covers sepsis during pregnancy, including its definition, risk factors, and unique pathophysiology. It emphasizes early detection through tailored screening tools, diagnostic methods, and management strategies like antibiotic administration and supportive therapies.

Definition

In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock Task Force highlighted that sepsis should be viewed as a manifestation of organ dysfunction rather than solely as a sign of infection. Sepsis 3 defined it as "a life-threatening condition of organ dysfunction resulting from an abnormal host response to infection (Kim et al., 2018; Shields et al., 2023). Organ dysfunction can be assessed objectively through a 2-point rise in the Sequential Organ Failure Assessment (SOFA) score (Shields et al., 2023). The Septic Shock Task Force describes septic shock as a state of sepsis marked by profound circulatory and cellular/metabolic impairment, which leads to a substantial rise in mortality rates (Shields et al., 2023). The Sepsis-3 definition characterizes septic shock as a clinical condition of sepsis involving sustained hypotension that necessitates vasopressors to achieve a MAP of ≥65 mmHg, in the absence of hypovolemia, alongside a serum lactate level exceeding 2 mmol/L even after sufficient fluid resuscitation (Kim et al., 2018; Shields et al., 2023).

Epidemiology

WHO estimates that maternal sepsis affects 4.4% of live births globally, amounting to approximately 5.7 million cases annually (Fan et al., 2020; Greer et al., 2020; Parfitt & Hering, 2018). The CDC reports that maternal sepsis ranks as the second most common cause of maternal mortality, responsible for 13.9% of all maternal deaths, with a mortality rate of 2.2 per 100,000 live births (Bauer et al., 2019; Bridwell et al., 2019; Fan et al., 2020; Shields et al., 2023). The mortality rate for obstetric infections complicated by severe sepsis or septic shock is estimated to be between 12% and 28% (Bridwell et al., 2019). The risk of sepsis during childbirth and the postpartum phase is 2 to 3 times greater than during the antenatal period (Fan et al., 2020). Women over 35, smokers, and Black women are more susceptible to maternal sepsis. Smoking during pregnancy is linked to harmful maternal and neonatal outcomes. Even smoking in early trimesters increases risks, highlighting the importance of cessation before pregnancy (Bacheller et al., 2021) Cigarette smoking status and cumulative smoking amounts are independently linked to a higher risk of sepsis, with heavy former smokers facing greater risks than non-smokers (Lee et al., 2024). Smoking during pregnancy is widely recognized to increase the risk of preterm premature rupture of membranes (PPROM), preterm birth, low birth weight, placenta previa, and placental abruption, all of which can contribute to maternal sepsis (Roelands et al., 2009). Black women face a three to four times higher risk of pregnancy-related deaths than white women. Improving healthcare quality across all stages of care may help improve outcomes for racial and ethnic minority women (Howell, 2018). For instance,

additional maternal health conditions, urinary tract infections, dysuria, and multiple symptoms were identified as key predictors of maternal sepsis in Ghana (Noora et al., 2022).

The fetus faces an increased likelihood of miscarriage, stillbirth, and preterm delivery. In high-income countries, maternal sepsis accounts for 10-25% of stillbirths, with this figure potentially rising to 50% in low- and middle-income nations (Greer et al., 2020). Women admitted during the postpartum or post-abortion period in low-income countries are at a greater risk of severe maternal complications compared to those in upper-middle-income or high-income countries (Brizuela et al., 2021). Maternal sepsis causes high morbidity and mortality in resource-limited settings due to limited diagnostic tools and treatment options, leading to deaths, ICU admissions, and intubations (Abera et al., 2024). Health system gaps worsen the management of maternal infections in low-income compared to high-income countries. Tools like obstetrically modified quick SOFA help, but resource and specialist shortages still endanger women with maternal sepsis (Maswime & Buga, 2021).

Between 1990 and 2019, the global age-standardized rates of maternal sepsis and other maternal infections among women of childbearing age decreased significantly, highlighting improvements in the treatment and management of these conditions (Chen et al., 2021). From 2020 to 2044, a decline in age-standardized incidence, mortality rates, and deaths is projected. This improvement can also be attributed to advancements in diagnostic and treatment practices, which enhance patient outcomes, alongside better health education for pregnant women, potentially reducing the future disease burden. Additionally, a related study predicted a global decline in fertility rates, from a total fertility rate (TFR) of 2.21 in 2022 to 1.83 by 2050, which could reduce the future disease burden of maternal sepsis and other maternal infections (Bhattacharjee et al., 2024).

Sources of Infection

During pregnancy, the immune response of the mother adjusts to prevent fetal rejection, but these alterations can also increase vulnerability to infections (Fan et al., 2020; Fernández-Pérez, Salman, Pendem, & Farmer, 2005). Infections leading to maternal sepsis can stem from pelvic or non-pelvic sources (Shields et al., 2023).

Pelvic Sources

In obstetric patients, common infection sources are the urinary tract, kidneys, and uterus (Parfitt & Hering, 2018; Shields et al., 2023). Chorioamnionitis, and endometritis account for about 59% of sepsis cases (Bauer et al., 2019). Maternal sepsis can be caused by obstetric factors like uterine infections (chorioamnionitis, endometritis), septic abortion, retained placenta, pelvic abscesses, and wound infections. Invasive procedures like amniocentesis and cerclage can also lead to sepsis. Invasive procedures can result in sepsis by creating an entry point for bacteria or fungi to enter the body, either during or after the procedure. Reducing the surgical stress response likely improves patient outcomes. Modifiable factors contributing to postoperative immune suppression include the use of minimally invasive surgery, and the avoidance of hemorrhage, blood transfusions, and perioperative bacterial contamination (MacFie, 2013).

A French study found chorioamnionitis as the leading cause of bacteremia (Fan et al., 2020). Pregnancies complicated by chorioamnionitis have a high rate of severe adverse outcomes, affecting 1 in 20 cases. These pregnancies also carry nearly a three-fold higher risk of requiring maternal intensive care unit admission compared to those without chorioamnionitis (Perry, Rossi, & DeFranco, 2019). Chorioamnionitis is a frequent pregnancy infection, often occurring in cases of prolonged pre-labor rupture of membranes (PROM) or during labor (Shittu et al., 2021). Chorioamnionitis is typically a polymicrobial infection, involving both anaerobic and aerobic bacteria, often originating from the vaginal flora. It generally occurs when bacteria ascend from the lower genital tract into the usually sterile amniotic cavity. The development,

progression, and resolution of such infections may be associated with vaginal dysbiosis (Lukanović et al., 2023).

Non-pelvic Sources

Maternal sepsis can also originate from non-pelvic sources, including respiratory infections like bacterial or viral pneumonia and tuberculosis. Conditions within the abdomen, such as a ruptured appendix, acute appendicitis, acute cholecystitis, and bowel infarction, may contribute as well. Other contributing factors include breast infections, septic pelvic thrombophlebitis, necrotizing fasciitis, malaria, and miliary tuberculosis (Elton & Chaudhari, 2015). Non-obstetric causes include pyelonephritis and pneumonia (Fan et al., 2020). Pneumonia accounts for 30% of infections in pregnant patients with severe sepsis, posing considerable risks to both the mother and fetus (Bridwell et al., 2019). Maternal sepsis can also result from critical obstetric conditions like heavy bleeding, embolism, AFLP, heart failure, cardiopulmonary arrest, and severe trauma. Postpartum infections such as wound infections, necrotizing fasciitis, toxic shock syndrome, gas gangrene, septic pelvic thrombophlebitis, pyogenic sacroiliitis, and *C. difficile* colitis can also lead to sepsis (Bauer et al., 2019).

Microorganisms Responsible for the Infection

Commonly reported pathogens include *Escherichia coli*, Group A and B *Streptococcus*, *Staphylococcus*, and Gram-negative bacteria (Bauer et al., 2019; Fan et al., 2020; Shields et al., 2023). Group A *β-hemolytic streptococcus* (GABHS) is a cause of maternal sepsis following abortion or delivery and is frequently associated with shock, resulting in a mortality rate of 30-60% (Fan et al., 2020; Parfitt & Hering, 2018). *Candida*-induced maternal sepsis can result in complications like chorioamnionitis, stillbirth, miscarriage, preterm labor, and congenital infections in newborns. Rare pathogens identified in maternal sepsis include *Clostridium innocuum*, *Clostridium novyi*, *Plasmodium vivax*, and *Chlamydia psittacosis* (Fan et al., 2020). Polymicrobial infections can also occur, with about 15% of maternal deaths from sepsis having identifiable causes attributed to mixed infections (Shields et al., 2023).

Risk Factors

Pregnancy may serve as a contributing factor to the development of sepsis (Fernández-Pérez et al., 2005; Parfitt & Hering, 2018). Pregnancy-induced systemic changes increase susceptibility to infections, including immune suppression to prevent fetal rejection. (Parfitt & Hering, 2018). Sepsis risk factors include prenatal risks like being a first-time mother, non-Caucasian ethnicity, poor antenatal care, obesity, anemia, diabetes, chronic hypertension, and recent antibiotic use. Intrapartum risks, such as unplanned cesarean sections, prolonged labor, and excessive vaginal exams, increase infection likelihood. Postpartum risks include retained placental fragments and breast issues like cracked nipples and mastitis (Fan et al., 2020; Parfitt & Hering, 2018).

Pathogenesis and Pathophysiology of Sepsis

Sepsis results from an abnormal immune response to infection, causing widespread damage to multiple organ systems (Shields et al., 2023). Sepsis triggers both pro-inflammatory and anti-inflammatory responses while also altering non-immunological pathways, including those related to cardiovascular, neurological, autonomic, hormonal, bioenergetic, metabolic, and coagulation functions (Fan et al., 2020). Multiorgan failure in sepsis begins with disrupted inflammation, causing excessive release of inflammatory mediators like TNF-α, IL-1, and complement proteins. Anti-inflammatory mediators like IL-4 and IL-10 are also released, potentially leading to immunosuppression. This results in endothelial dysfunction, impaired oxygen exchange, vasodilation, low blood pressure, and increased capillary permeability (Parfitt & Hering, 2018). Systemic inflammation drives multiorgan failure in sepsis through microvascular and mitochondrial dysfunction. Septic shock, marked by hypovolemia, cardiac

dysfunction, and vasodilation, progresses from early hypovolemia to vascular and myocardial dysfunction. Leukocyte activation increases capillary permeability, causing edema. Sepsis impacts multiple organ systems: respiratory (34%), cardiovascular (12%), liver and GI (10%), kidneys (16%), hematologic (19%), endocrine, and CNS (8%).

Clinical Manifestations

Pregnancy can complicate sepsis diagnosis due to changes that mask SIRS indicators. Symptoms like malaise, shortness of breath, back pain, cramps, abdominal pain, nausea, vomiting, and fever overlap with normal pregnancy signs. Elevated leukocyte counts during pregnancy are not reliable. Signs of maternal sepsis include temperature >38°C or <36°C, pulse >110 bpm, respiratory rate >24 breaths/min, hypotension (systolic BP <90 mmHg or MAP <70 mmHg), extreme leukocyte count, and clotting issues (Parfitt et al., 2017). Sepsis symptoms vary by infection source, like cough in pneumonia or wound discharge in abscesses. Early skin warmth turns cold in shock. Hypoperfusion signs include slow capillary refill, cyanosis, mental changes, fatigue, oliguria, and ileus. Factors like age, diabetes, and medications can affect symptoms. Abdominal pain, tachycardia, and elevated lactate in pregnant or postpartum patients are alarming (Fernández-Pérez et al., 2005; Parfitt & Hering, 2018).

Diagnosis of Sepsis

Timely sepsis detection in pregnancy and postpartum is crucial to reducing morbidity and mortality. The Society for Maternal-Fetal Medicine (SMFM) advises considering sepsis in pregnant or postpartum patients with unexplained organ damage, especially with suspected or confirmed infection, even without fever (Shields et al., 2023). Key diagnostic steps for sepsis involve blood cultures, site-specific infection cultures, supplementary lab tests, and imaging to identify the infection's anatomical location (Fan et al., 2020).

Sepsis Screening Instruments in Pregnancy

Quick Sequential [Sepsis-Related] Organ Failure Assessment (qSOFA)

qSOFA helps identify sepsis, assess disease severity, and predict mortality risk in ICU patients with infections (Bauer et al., 2019; Parfitt & Hering, 2018; Shields et al., 2023; Small et al., 2020). qSOFA assesses three criteria: systolic blood pressure ≤100 mmHg, respiratory rate >22/min, and changes in mental status (Parfitt et al., 2017; Shields et al., 2023). Sepsis and a suspected infection are confirmed when 2 of the 3 criteria are present. A higher SOFA score is associated with a greater risk of adverse sepsis outcomes and a 3-14 times higher likelihood of hospital death (Fan et al., 2020; Parfitt & Hering, 2018; Shields et al., 2023; Small et al., 2020). Studies indicate that qSOFA has low sensitivity and high specificity (29.9% vs 96.1%) for bedside sepsis screening (Shields et al., 2023). A recent meta-analysis found that SIRS has better sensitivity, while qSOFA is more specific (Bauer et al., 2019). Physiological differences make qSOFA and SOFA challenging to apply in pregnant or postpartum women, with no external validation for this group. Pregnancy affects SOFA criteria like creatinine and MAP, with creatinine >1.2 mg/dL being abnormal and MAP <70 typical in the second trimester. Sepsis thresholds for respiratory rate, heart rate, CO2, and white blood cell count often overlap with normal pregnancy and postpartum ranges (Bridwell et al., 2019; Greer et al., 2020).

Systemic Inflammatory Response Score (SIRS)

SIRS helps identify sepsis by evaluating three clinical parameters and one lab test: temperature <36°C or >38°C, respiratory rate >22/min, heart rate >90 bpm, and white blood cell count <4000 or >12000. Sepsis is diagnosed when two or more criteria are met and infection is suspected. SIRS is less specific for sepsis. A study of 270,000 hospitalized patients found nearly half met two or more SIRS criteria. Leukocytosis and fever, often seen after surgery, are also part of SIRS (Small et al., 2020). SIRS has a sensitivity of 93%, but its specificity is only 63%, leading to potential false alarms (Bauer et al., 2019).

Modified obstetric early warning scoring systems (MOEW)

In 2016, the Maternal Early Warning Trigger tool was introduced to quickly assess obstetric patients at high risk of sepsis, cardiopulmonary issues, hypertension, and bleeding (Bauer et al., 2019; Greer et al., 2020; Parfitt & Hering, 2018). The Maternal Early Warning Trigger tool monitors vital signs, oxygen levels, mental state, pain, and fetal heart rate to detect early clinical deterioration. Evaluation is required if two or more non-severe triggers or one severe trigger are noted (Greer et al., 2020; Parfitt & Hering, 2018). Maternal non-severe abnormal triggers include temperature ≥38°C or ≤36°C, oxygen saturation ≤93%, heart rate >110 or <50 bpm, respiratory rate >24 or <12 bpm, BP abnormalities, mental status changes, and fetal heart rate >160 bpm. Severe triggers include heart rate >130 bpm, respiratory rate >30, MAP <55 mmHg, and oxygen saturation <90%. If two non-severe triggers or one severe trigger occur, a complete blood count and blood culture should be performed (Parfitt et al., 2017).

Sepsis in Obstetrics Score (SOS)

The SOS system, introduced in 2014, is an obstetric assessment tool that considers physiological changes in the cardiovascular, respiratory, and immune systems during pregnancy to assess the need for ICU admission. A score of 6 or higher was found to be more effective in predicting ICU admission than individual variables and other early warning scores (Greer et al., 2020).One study showed a positive predictive value of 16.7%, sensitivity of 64%, specificity of 88%, and a negative predictive value of 98.6% (Shields et al., 2023).

California Maternal Quality Care Collaborative [CMQCC] 2-step process

The CMQCC uses a two-step screening process. Step 1 assigns points for abnormal vital signs like temperature <36°C or >38°C, heart rate >100 bpm for 15 minutes, respiratory rate >24 bpm for 15 minutes, and abnormal leukocyte count. A positive result occurs if 2 out of 4 criteria are met. Step 2 confirms organ dysfunction with clinical and laboratory evaluation. The screening has 97% sensitivity and 99% specificity (Shields et al., 2023).

Polymerase Chain Reaction (PCR) and Mass Spectrometry

Multiplex PCR detects pathogen DNA and resistance genes from blood cultures and samples but requires further validation for widespread use. MALDI-TOF mass spectrometry identifies various organisms from positive cultures with speed and accuracy. NICE currently recommends PCR for diagnosing meningococcal meningitis in children (Greer et al., 2020).

Biomarkers

C-reactive protein (CRP)

CRP rises in conditions like infections and surgery, with 81% sensitivity and 67% specificity for bacterial infections. Its low specificity limits its use in diagnosing sepsis, though it helps monitor treatment (Greer et al., 2020).

Procalcitonin (PCT)

PCT, released during infection, is more specific (81%) than CRP (67%) for bacterial infections. While useful for early sepsis diagnosis (77% sensitivity, 79% specificity), its role is limited as it can rise after surgery or cardiogenic shock. NICE and SSC guidelines do not recommend routine PCT use for guiding treatment due to insufficient evidence (Greer et al., 2020).

Lactate

A lactate level >2 mmol/L signals the need for critical care and is a marker for septic shock under Sepsis-3 criteria. The 3-hour bundle recommends lactate measurement within 3 hours. In pregnancy, lactate may rise due to increased metabolic demands. Elevated lactate in pregnant women indicates poor outcomes, and levels >4 mmol/L in non-pregnant women with septic

shock are linked to 46% mortality. Metabolic acidosis should also be measured (Greer et al., 2020).

Culture

Blood cultures should be collected before starting antimicrobial treatment. While pathogen identification supports the diagnosis, it's not always required, as 50% of sepsis cases have negative cultures. Cultures from all potential infection sources, including blood, cerebrospinal fluid, urine, wound exudate, and respiratory secretions, should be taken without delaying therapy. Two sets of blood cultures (aerobic and anaerobic) are recommended for suspected sepsis cases (Parfitt & Hering, 2018).

Sepsis Treatment

Sepsis management emphasizes early identification and supportive care (Greer et al., 2020). The primary goal of therapy for obstetric patients is to resuscitate the mother, restore intravascular volume, initiate appropriate antibiotics, and identify the infection source (Parfitt & Hering, 2018).

Fluid Resuscitation

Fluid resuscitation is crucial for hypotension in sepsis, but aggressive fluid administration without monitoring can cause pulmonary and cerebral edema, and increase intra-abdominal pressure, worsening mortality (Shields et al., 2023). The 2021 SSC guidelines recommend initial intravenous fluid resuscitation at a rate of 30 ml/kg within the first 3 hours (Greer et al., 2020; Shields et al., 2023). This recommendation was adjusted to 20 ml/kg by the RCOG (Royal College of Obstetricians and Gynecologists) due to the increased risk of pulmonary edema during pregnancy caused by a decrease in colloid oncotic pressure (Greer et al., 2020; Parfitt & Hering, 2018; Shields et al., 2023). This should be initiated without delay for the management of septic shock when blood lactate levels are >4 mmol/L and/or to achieve a MAP >65 mmHg (Greer et al., 2020). Society for Maternal-Fetal Medicine (SMFM) recommends early intravenous fluid administration (within the first 3 hours) of 1-2 L of crystalloids for sepsis with complications of hypotension or suspected organ hypoperfusion (Shields et al., 2023). Albumin is second-line after crystalloids due to cost. The 6S trial showed HES increased mortality and renal therapy, leading to discontinuation. Obstetric patients should maintain urine output of at least 0.5 mL/kg (Parfitt & Hering, 2018; Shields et al., 2023). After resuscitation, assessing response is crucial. CVP is unreliable; dynamic measurements like pulse-pressure variation or echocardiography can lower mortality (Shields et al., 2023). To prevent inferior vena cava compression, the patient should be positioned in the left lateral decubitus position during passive leg raising (Parfitt & Hering, 2018). After 2-3 minutes, fluid-responsive patients will show increased cardiac output, while those with no improvement may be better treated with vasopressors (Shields et al., 2023).

Control of Infection Source

Identifying the source of infection should be part of the initial and ongoing treatment for sepsis patients (Parfitt & Hering, 2018). Interventions to control infection include removal of foreign bodies, catheters, and devices that may worsen the condition; drainage and debridement of injuries or wounds; and correction of metabolic processes that cause ongoing contamination (Fan et al., 2020; Parfitt & Hering, 2018). Infection source control requires prompt antibiotics. SSC recommends a two-antibiotic combination for septic shock, adjusted by local susceptibility. If ineffective, abscess drainage or source removal is needed. Delays in control increase 28-day mortality, with each 6-hour delay raising rates (Fan et al., 2020).

Antibiotic Management

IV antibiotics should be given within 1 hour of septic shock symptoms (Evans et al., 2021). Blood cultures should be taken before antibiotics are administered. Early combination therapy with broad-spectrum antibiotics is recommended. (Fan et al., 2020; Shields et al., 2023). For pregnant or postpartum patients with septic shock or suspected sepsis, SSC strongly recommends administering broad-spectrum empirical antimicrobials within 1 hour of sepsis diagnosis (Bridwell et al., 2019; Shields et al., 2023). Infections that lead to maternal sepsis are often polymicrobial, thus initial antimicrobial treatment for maternal sepsis should include broad-spectrum antibiotics covering gram-positive, gram-negative, aerobic, and anaerobic bacteria (Fan et al., 2020; Shields et al., 2023). Combination therapy is preferred over monotherapy (Fan et al., 2020; Rhee et al., 2020). Common options include broad-spectrum carbapenems (meropenem, imipenem/cilastatin, doripenem) or long-acting penicillin/beta-lactamase inhibitor combinations (piperacillin/tazobactam, ticarcillin/clavulanate).

Carbapenem antibiotics are highly effective against infections caused by resistant bacteria. They belong to the β-lactam class, which includes penicillins, cephalosporins, and monobactams. Carbapenems are known for their broader spectrum of activity compared to other β-lactams, making them effective against both Gram-positive and Gram-negative bacteria. These antibiotics have a similar molecular structure to other β-lactams, and their stability is enhanced by their resistance to enzymes that typically inactivate β-lactams (Aurilio et al., 2022). The pharmacokinetics of beta-lactam antibiotics are known to change during pregnancy, with faster elimination and reduced plasma concentrations. However, the use of prolonged beta-lactam infusions in treating maternal sepsis has not been thoroughly researched. It is considered best practice to adjust antimicrobial dosing strategies according to established pharmacokinetic and pharmacodynamic principles, as well as the specific characteristics of the drug (Shields et al., 2023). The latest SSC guidelines recommend prolonged beta-lactam infusions after the initial bolus, as they reduce short-term mortality in sepsis and septic shock (Shields et al., 2023).

Third-generation cephalosporins may also be used in multi-drug regimens (Fan et al., 2020). Cephalosporins are a flexible group of β-lactam antibiotics that have been commonly used for decades to treat bacterial infections. With five generations of development, they have shown effectiveness against a broad variety of pathogens, covering both Gram-positive and Gram-negative bacteria. Third-generation cephalosporins, such as ceftriaxone, cefotaxime, cefpodoxime, and ceftazidime, provide extended coverage against Gram-negative bacteria, especially those resistant to first- and second-generation cephalosporins. Cephalosporins are bactericidal antibiotics that work by interfering with bacterial cell wall synthesis, ultimately causing the death of the bacteria (Karunarathna et al., 2024).

For pregnant or postpartum patients with sepsis or septic shock at high risk for methicillin-resistant Staphylococcus aureus (MRSA), broad-spectrum antibiotics with MRSA activity are recommended. If there is a high risk of multidrug resistance, using two antimicrobials with gram-negative coverage is preferred over a single gram-negative agent. Empiric coverage recommendations may evolve as antibiotic resistance continues to spread (Shields et al., 2023).

Antibiotic allergies, especially in obstetrics and gynecology, present challenges, particularly in cases of maternal sepsis, as beta-lactam antibiotics are first-line treatments. Using alternative antibiotics can lead to increased complications, longer hospital stays, and antibiotic resistance. While true penicillin allergies are rare, many patients tolerate penicillin despite reported allergies. Allergy evaluations, including patient history, skin testing, and oral challenges, are safe and effective, even in pregnancy. These assessments help guide the use of first-line antibiotics. Cross-reactivity between penicillin and cephalosporins is low, and guidelines recommend cephalosporins for patients with non-anaphylactic penicillin allergies. In cases of

no alternative, desensitization can be performed. Cephalosporin and metronidazole allergies are managed with skin testing or desensitization, depending on the risk. Obstetricians and gynecologists should identify and refer patients with reported allergies for further evaluation, which is essential for effective antibiotic stewardship (Burn et al., 2024).

Antimicrobial stewardship is essential in managing pregnant or postpartum patients with sepsis. While the optimal treatment duration remains unclear, studies in non-obstetric patients suggest that shorter courses of therapy are equally effective and cause fewer side effects. However, limited research exists for critically ill sepsis patients (Shields et al., 2023). The optimal duration of antibiotics is debated, with the SSC recommending 7-10 days (Fan et al., 2020). Current SSC guidelines recommend daily evaluation to potentially de-escalate antimicrobial use (Shields et al., 2023). Procalcitonin levels can serve as a biomarker to guide the initiation, de-escalation, and discontinuation of antimicrobial therapy (Fan et al., 2020).

Vasoactive Agents

In patients with hypotension who do not respond to fluids or are not candidates for further fluid resuscitation, vasopressors, and inotropes are used to increase blood pressure and improve heart contractility (Evans et al., 2021; Parfitt & Hering, 2018; Shields et al., 2023). Vasopressors can be used in pregnant women with septic shock to constrict the pathologically dilated systemic circulation and maintain adequate perfusion (Shields et al., 2023). Guidelines recommend norepinephrine as the first-line medication with an initial target MAP of 65 mmHg (Evans et al., 2021; Greer et al., 2020; Shields et al., 2023). Norepinephrine appears safe for the fetus at low doses, although the MAP threshold in pregnant women has not been fully studied (Parfitt & Hering, 2018; Shields et al., 2023). Vasopressin or epinephrine is considered second-line after norepinephrine for refractory shock, with fetal monitoring recommended once viable. In myocardial dysfunction with persistent hypoperfusion, dobutamine can be added to norepinephrine, or epinephrine can be used alone (Parfitt & Hering, 2018; Shields et al., 2023). Catecholamines, particularly dopamine, can cause arrhythmias, and vasopressin may help reduce their dosage. Inotropes are considered when cardiac output is impaired due to sepsis (Greer et al., 2020). Phenylephrine and ephedrine are second-line options but can cause tachyphylaxis. Phenylephrine does not affect fetal acid-base status, though it may cause maternal bradycardia and reduced cardiac output. Dobutamine is preferred for septic myocarditis (Bridwell et al., 2019).

Glycemic Control

During labor, glucose levels are kept between 80-120 mg/dL to prevent fetal hypoglycemia or hyperglycemia. Ketoacidosis in the mother can reduce fetal oxygenation and perfusion (Parfitt & Hering, 2018). Maternal blood glucose levels should be kept below 180 mg/dL to reduce adverse effects on the baby. Hyperglycemia (>180 mg/dL) is associated with increased mortality in critically ill patients. SMFM recommends insulin therapy for glucose levels >180 mg/dL in pregnant women with sepsis (Shields et al., 2023).

Steroids

The use of intravenous steroids for sepsis and septic shock remains controversial (Greer et al., 2020). The SSC 2012 and 2016 guidelines recommend intravenous hydrocortisone at 200 mg/day (50 mg every 6 hours or as a continuous infusion) for 7 days, discontinued after clinical improvement. The SMFM advises IV corticosteroids for pregnant or postpartum patients with septic shock who continue to require vasopressor therapy (Shields et al., 2023).

Oxygen

Oxygen should be administered to achieve a saturation of ≥94%, with a target SvO2 ≥65% or ScvO2 ≥70% in critically ill patients, similar to the general population. In the third trimester of

pregnancy, SvO2 is around 80%, but evidence regarding the optimal SvO2 in critically ill pregnant patients is limited (Greer et al., 2020).

Intravenous Immunoglobulin

Intravenous immunoglobulin (IVIg) is rarely used but may be an adjunctive therapy for severe invasive staphylococcal and streptococcal sepsis. Evidence on its benefits in pregnancy-related sepsis is limited, though an RCT showed reduced morbidity and mortality with anti-endotoxin immunoglobulin in obstetric septic shock patients (Greer et al., 2020).

Extracorporeal Membranous Oxygenation (ECMO)

ECMO has been used in a small number of pregnant and postpartum patients with heart or respiratory failure due to severe sepsis and septic shock. The outcomes are generally positive, with satisfactory cardiac function recovery, a 70% fetal survival rate, and an 80% maternal survival rate (similar to non-pregnant women). ECMO may be considered for refractory sepsis treatment (Fan et al., 2020; Greer et al., 2020).

Additional Therapy

Stress ulcer prophylaxis is recommended for septic shock patients with bleeding risk factors, and DVT prevention is crucial for pregnant women with sepsis due to hypercoagulability. Prophylactic measures include compression stockings, intermittent leg compression, and heparin. Adjunctive therapies include red blood cell transfusion for hemoglobin <7 g/dL and platelet infusion for counts between 5,000-30,000/μL to prevent bleeding (Parfitt & Hering, 2018).

Considerations For the Fetus

It is crucial to stabilize the mother's condition first, as this will subsequently improve the fetal status (Fan et al., 2020). Fetal heart rate monitoring should be continuous once the pregnancy is considered viable. Maternal hyperventilation should be avoided as it can reduce blood flow to the uterus and placenta, potentially lowering the fetal pH (Parfitt & Hering, 2018). If the source of infection is outside the uterus, efforts should focus on treating the mother's sepsis and prolonging the pregnancy. However, if the source of sepsis is from the uterus, delivery should be performed (Fan et al., 2020).

Complications

Severe pregnancy-related sepsis can lead to organ dysfunction in mothers, including pulmonary edema and myocardial ischemia, as well as preterm labor and neonatal complications. In ICU patients with SIRS, there is a higher risk of organ failure and maternal death. Neonatal sepsis, despite treatment, still results in high rates of death or disability (Bonet et al., 2018).

Prognosis

Delayed identification and treatment of sepsis lead to worse outcomes. Septic shock increases ICU mortality to 20-28%, with poor response to IV fluids, tissue hypoxia, myocardial dysfunction, high lactate, and multi-organ failure. Mortality from multiple organ dysfunction rises to 90% with additional organ failure. Premature delivery is common in sepsis, especially with uterine bacteremia. Non-pelvic bacteremia can lead to miscarriage, early delivery, or delayed delivery. Post-sepsis complications like infertility may result from pelvic infections or hysterectomy (Parfitt et al., 2017; Shields et al., 2023).

Prevention

Preventing infection is key to reducing sepsis in mothers. Measures include education on infection signs, handwashing, using antiseptic soap before surgery, avoiding smoking before surgery, and controlling blood glucose in diabetics. Antibiotic prophylaxis during cesarean reduces infections like fever and wound infections. Antibiotics are also recommended for

premature rupture of membranes before 37 weeks and severe pelvic tears and can help reduce chorioamnionitis in meconium-stained amniotic fluid (Parfitt et al., 2017).

Conclusion

Sepsis is a leading cause of ICU admission and maternal morbidity and mortality. It can result from both obstetric and non-obstetric factors, with common pathogens including E. coli, Streptococcus, Staphylococcus, and other gram-negative bacteria. Pregnancy-related anatomical and physiological changes can delay sepsis recognition, leading to septic shock and organ dysfunction. Using tools like the Maternal Early Warning Trigger can help identify sepsis and guide management. Sepsis treatment in pregnancy should follow the same principles as in non-pregnant populations, including early recognition, fluid therapy, timely antibiotics, and source control.

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