



Review Article

Volume 23 Issue 5 - August 2022
DOI: 10.19080/JGWH.2022.23.556125

J Gynecol Women's Health

Copyright © All rights are reserved by Warren Carll

Sepsis and Pregnancy



Warren Carll^{1,2*}, Richard W Carlson^{1,3,4}, Anthony Vaccarello^{1,2} and Ashlye Carll⁵

¹Department of medicine, Valleywise Medical Center, United States

²Creighton University School of Medicine, United States

³College of Medicine, University of Arizona, United States

⁴Mayo Clinic Alix School of Medicine, United States

⁵Phoenix Children's Hospital, United States

Submission: August 18, 2022; **Published:** August 25, 2022

***Corresponding author:** Warren Carll, Creighton University School of Medicine, Phoenix, AZ, United States

Abstract

Sepsis continues to be a leading cause of morbidity and mortality in pregnant patients. Despite advances in sepsis screening, diagnosis, and management, mortality has been increasing around the world. In this review, we discuss the advances in the screening, diagnosis, and management of sepsis in pregnant patients. We also discuss areas for potential improvement.

Keywords: Sepsis; Septic shock; Pregnancy; Sepsis management; Sepsis screening

Abbreviations: MAP: Mean Arterial Pressure; SIRS: Systemic Inflammatory Response Syndrome; SOFA: Sequential Organ Failure Assessment; ICU: Intensive Care Unit; ECMO: Extracorporeal Membranous Oxygenation; MEW: Maternal Early Warning

Introduction

In the most recent SEPSIS-3 criteria, sepsis was defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection; and septic shock was defined as persistent hypotension and an elevated lactic acid $>2\text{mmol/L}$ in the absence of hypovolemia and requiring vasopressors to maintain a mean arterial pressure (MAP) of $\geq 65\text{mmHg}$. Rather than utilizing the traditional systemic inflammatory response syndrome (SIRS) criteria, SEPSIS-3 focuses on the use of the quick Sequential Organ Failure Assessment (qSOFA) score outside of the intensive care unit (ICU), and the SOFA score for the ICU. The primary rationales for this paradigm shift are that these definitions are less ambiguous, easier to incorporate at the bedside, more rapid than waiting for laboratory studies, and can be assessed anywhere rapidly at the bedside, even without laboratory or imaging capabilities [1]. This is important, as sepsis remains a major cause of pregnancy-related morbidity and mortality. In fact, the incidence of sepsis in pregnancy has increased by 236% in the United States and remains the 3rd most common maternal cause of death in the peripartum period globally. This is thought to be due to barriers to care of the pregnant patient, along with failure to recognize sepsis in these patients [2].

Pathophysiology

Sepsis is a multifaceted host response to infection, with activation of both pro-, and anti-inflammatory pathways. Additionally, there is modification of many non-immune physiological pathways, including cardiovascular, endocrine, coagulation, hormonal, and autonomic; all of which have prognostic significance. In fact, mortality increases significantly with each system affected. This may result in increased risk of premature rupture of membranes, neurodevelopmental abnormalities, such as cerebral palsy, premature labor, stillbirth, and maternal mortality [3-6]. During pregnancy, there are multiple adaptations to the maternal immune system to prevent immune rejection of the developing fetus, which are beyond the scope of this article. These must be balanced to allow for adequate host response to infection [8]. Well-described risk factors for sepsis during pregnancy include invasive procedures, such as cervical cerclage and amniocentesis, cesarean delivery, mastitis, lack of prenatal care, immunosuppression, poverty, and obesity [8,9]. The most common sources of sepsis in this population include pyelonephritis and pneumonia, followed by chorioamnionitis/

endometritis, gastrointestinal tract trauma or rupture, and retained products of conception [10].

Pathogens

The most commonly implicated pathogens in sepsis are bacterial. These include gram negative organisms, such as Escherichia coli, along with Streptococcus and Staphylococcus [11]. Although rare, group A Streptococcus may be an important cause of shock and death in the pregnant patient, with a reported mortality of 30-60% [12]. This is largely due to the organism's ability to spread through tissue planes, resulting in necrotizing soft tissue infections. Additionally, exotoxin production may lead to toxic shock syndrome. Occasionally, Candida species can lead to sepsis, especially in the immunocompromised patient. Important viral causes of sepsis include Influenza A and B, and CoVID-19 [10,13]. Of particular interest is CoVID-19, as pregnant patients with CoVID-19 may be at a higher risk of more severe disease. Pregnancy-related complications of CoVID-19 include increased risk of preterm delivery and venous thromboembolism [13].

Screening and Diagnosis

Several warning signs of sepsis in pregnancy have been developed. According to Bauer et al., the Systemic Inflammatory Response Syndrome (SIRS) was the most sensitive and least specific, whereas the quick Sequential Organ Failure Assessment (qSOFA) was the most specific and least sensitive screening tool. Maternal early warning (MEW) was less sensitive than SIRS and less specific than qSOFA [14]. In Australia and New Zealand, omqSOFA has recently been adopted to help aid in the identification of sepsis in pregnant patients, as there are important physiologic changes during pregnancy. The most relevant physiological changes during pregnancy include increased minute ventilation and hypotension, particularly during the 3rd trimester due to the gravid uterus compromising venous return. It is unknown whether these criteria improve sensitivity and specificity of qSOFA in the pregnant patient [15]. (Table 1) compares and contrasts SIRS, qSOFA, MEW, and omqSOFA.

Table 1: Comparison of SIRS, qSOFA, MEW, and omqSOFA in the detection of sepsis in pregnancy [14, 15].

| Term | Definition | Sensitivity | Specificity |
|--|---|-------------|-------------|
| SIRS | >/= 2 of the following: | 0.93 | 0.63 |
| | 1. Temperature: >38C, <36C | | |
| | 2. Heart rate: > 90 | | |
| | 3. Respiratory rate: >20 breaths/minute | | |
| | 4. white blood cell count >12x10 ⁹ or <4x10 ⁹ | | |
| qSOFA | >/= 2 of the following: | 0.5 | 0.95 |
| | 1. Respiratory rate: >/= 22 breaths/minute | | |
| | 2. Altered mentation | | |
| | 3. Systolic blood pressure </= 100mmHg | | |
| MEW | >/= 1 of the following: | 0.82 | 0.87 |
| | 1. Systolic blood pressure: <90 or >160mmHg | | |
| | 2. Diastolic blood pressure >120mmHg | | |
| | 3. Heart rate: <50 or >120 beats/minute | | |
| | 4. Respiratory rate: <10 or >30 per minute | | |
| | 5. Oxygen saturation <95% | | |
| | 6. Oliguria <35mL/h for >/= 22 hours | | |
| | 7. Alteration in mental status | | |
| 8. Pre-eclampsia with nonremitting headache or dyspnea | | | |

| | | | |
|----------------|--|---------|---------|
| omqSOFA | >/= 2 of the following: | Unknown | Unknown |
| | 1. Systolic blood pressure: <90mmHg | | |
| | 2. Respiratory rate: > 25 breaths/minute | | |
| | 3. Altered mentation | | |

Table definitions: SIRS-Systemic Inflammatory Response Syndrome. qSOFA-quick Sequential Organ Failure Assessment. SOFA-Sequential Organ Failure Assessment. omqSOFA-Obstetrically-modified quick Sequential Organ Failure Assessment.

Management

There are no differences in the management of sepsis in pregnant patients in the Surviving Sepsis Campaign. These guidelines were updated in 2018 to reflect the “Hour-1 Surviving Sepsis Campaign Bundle of Care”. The first priority within the first hour of presentation to the emergency department, or earliest recognition of sepsis, is to administer empiric antimicrobials after obtaining blood cultures. The most common pathogens include *Escherichia coli*, *Staphylococcus*, *Streptococcus*, and other gram-negative infections [1]. Blood cultures should not delay empiric antimicrobial administration, as mortality increases 7.6% each hour [16].

Other priorities include obtaining an initial blood lactate, with repeat assessments if the initial value >/= 2mmol/L, along with rapidly administering 30ml/kg of intravenous fluids for patients who are hypotensive and/or have a lactic acid >/= 4mmol/L. If the mean arterial pressure (MAP) remains <65mmHg, vasopressor therapy should be initiated. Additionally, a site of infection requiring source control should be sought and definitively managed [17]. In the pregnant patient, this should include delivery of the fetus if the uterus is thought to be the source of infection [2]. If the patient fails to respond to the above measures, Extracorporeal Membranous Oxygenation (ECMO) may be considered, as maternal and fetal survival rates with implementation of ECMO are 80% and 70%, respectively [18]. Finally, corticosteroids should be administered for patients <34 weeks of gestation, together with electronic fetal monitoring [19].

Discussion

As discussed herein, sepsis continues to be a significant cause of morbidity and mortality in pregnancy. Risk factors for sepsis in pregnancy include invasive procedures, cesarean delivery, immunosuppression, lack of preterm care, obesity, and lower socioeconomic status. The most common sources of infection in pregnancy include pneumonia and pyelonephritis, followed by chorioamnionitis/endometritis, retained products of infection, and gastrointestinal pathology. The most common organisms include *Escherichia coli* and other gram-negative organisms, as well as *Streptococcus* and *Staphylococcus*. Empiric antimicrobials targeting these organisms should be administered within the

first hour of recognition of sepsis, ideally after blood cultures have been obtained. A source of infection should be sought and aggressively managed.

In 2016, Chebbo et al. published a seminal review paper, which highlighted important topics regarding sepsis in pregnancy, including incidence and mortality, pathophysiology, current definitions, identification, prevention, sources of infection, and management of specific infections [20]. Since this paper was published, there have been additional changes in the understanding of sepsis in pregnancy, including definitions, scoring systems, and principles of management. There have also been advancements in the understanding of pathophysiology and risk factors of sepsis in the pregnant patient. The current emphasis is the use of empiric antimicrobials and aggressive management as soon as possible after the recognition of sepsis; ideally within the first hour. Despite these advances, rates of sepsis-related mortality have been increasing throughout the world. Future areas of improvement should therefore focus on barriers to care of the pregnant patient, along with early recognition.

Acknowledgements

Medical Intensive Care Unit staff of Valley wise Health Medical Center, April Aguinaga, MLS, AHIP. Valley wise Health Medical Center library.

References

- (2020) The WHO characterizes COVID-19 as a pandemic World Health Organization.
- (2020) Addressing the needs and leadership of women will strengthen the effectiveness of the response to COVID-19. UN Women.
- (2019) Activity, Employment and Unemployment Rate 2018. Women's Institute.
- Victoria A Ferrer-Perez (2020) Coping with the COVID-19 pandemic and its consequences from the vantage point of feminist social psychology (Facing the COVID-19 pandemic and its consequences from feminist Social Psychology). *International Journal of Social Psychology* 35(3): 639-646.
- Dino DiNella. Victoria Ibanez (2020) Causes and consequences of the COVID-19 pandemic. From the immobility of humanity to the decentralized circulation of people. *Rights in Action* 15(15): 407.
- Regional Directorate of Ayacucho-DIRESA-Ayacucho-Peru.

7. Raul Dominguez G, Alejandra E Cremonte, JLE Cendejas (2020) Latin American Association of Gynecological Endocrinology – ALEG. Position statement regarding the use of Combined Oral Contraceptives in patients with COVID-19 and high risk of thrombosis. TORREON, Coahuila.
8. Maria Solanas Cardin. The CoVID-19 crisis and its impacts on gender equality. Real Instituto Elcano Príncipe de Vergara, 51. 28006 Madrid (Spain).
9. Gerson E, Javier M, Waldo T, Ricardo A, J Amado (2020) Clinical-epidemiological characteristics of patients who died from covid-19 in a national hospital in Lima, Peru. *Rev Fac Med Hum* 20(2): 180-185.
10. Caparros-Gonzalez RA (2020) Maternal and neonatal consequences of COVID-19 coronavirus infection during pregnancy: a scoping review. *Rev Esp Public Health* 94: e202004033.
11. Huarcaya-Victoria J (2020) Considerations on mental health in the COVID-19 pandemic. *Rev Peru Med Exp Public Health* 37(2): 327-334.
12. Sola A, Rodriguez S, Cardetti M, Davila C (2020) Perinatal COVID-19 in Latin America. *Rev Panama Public Health* 44: e47.
13. Kably-Ambe A, Olavarria-Guadarrama MY, Sanchez AA, Roque-Sanchez AM, Alonso de MM, et al. (2020) COVID-19 and its repercussions on gynecological-obstetric practice. *Ginecol Obstet Mex* 88: 1-12.
14. Francis Collins, geneticist and director of the National Institutes of Health in the New England Journal of Medicine.
15. GUTIÉRREZ, Diana, Guillermina MARTIN and Hugo ÑOPO. The coronavirus and the challenges for women's work in Latin America. Lima: GRADE, 2020. (Research Documents, 110).
16. Deborah DP (2020) COVID-19 in Peru: A small technocracy facing the consequences of inequality. Carolina analysis.
17. Kably-Ambe A, Olavarria-Guadarrama MY, Sanchez Aranda A, Roque-Sanchez AM, Alonso de Mendieta M, Lopez-Marrufo. SARS-COV-2 (covid-19).
18. World Health Organization –WHO. conceptual definition of health.
19. Messing K (1996) Searching for the trail of the invisible: scientific indicators of women's occupational health risks. In: *Living in health making differences visible*. Madrid. Ministry of Social Affairs. Women's Institute.
20. Garcia Calvente MM (1997) The informal health care system during childhood [doctoral thesis]. Granada: University of Granada.
21. Duran MA (1986) The endless journey. Barcelona: Icaria.
22. Antolin L, Mazarrasa L (1997) Cooperation in health with a gender perspective. Madrid: Ed. Federation of Family Planning of Spain.
23. Rohlf, C. Borrell, C. Anitua L Artazcoz, C Colomer, et al. (2000) The importance of the gender perspective in health surveys. *Gac Sanit* 14(2): 146-155.



This work is licensed under Creative Commons Attribution 4.0 License
DOI: [10.19080/JGWH.2022.23.556125](https://doi.org/10.19080/JGWH.2022.23.556125)

Your next submission with Juniper Publishers will reach you the below assets

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats
(Pdf, E-pub, Full Tsex, Audio)
- Unceasing customer service

Track the below URL for one-step submission
<https://juniperpublishers.com/online-submission.php>