

SPECIAL ARTICLE**Gynecology**

Reducing post-cesarean sepsis: Current best practice in prevention and treatment

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Abstract

Cesarean section is the most common surgical procedure performed worldwide. It is associated with good perinatal and maternal outcomes when indicated. The rising global cesarean birth rate has coincided with an increase in post-cesarean sepsis – specifically site infections, which have an incidence of 7% worldwide. Post-cesarean sepsis remains a serious complication that prolongs hospital stays, resulting in additional surgery and worsening maternal morbidity and mortality, and increasing health-care costs with socioeconomic consequences. There is no global practice guide for

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post-cesarean sepsis, despite most maternal deaths due to sepsis occurring postpartum. Here we introduce a FIGO Committee on Infections During Pregnancy guide on prevention and treatment of post-cesarean sepsis. We encourage strategies to keep cesarean birth rates at evidence-based levels by aiming to standardize the management of labor and to increase the percentage of vaginal births after a previous cesarean. Identification of risk factors before and during the surgery is the primary step towards prevention. These measures, combined with evidence-based strategies to promote infection prevention practices, including routine prophylactic antibiotics, skin and vaginal preparation before cesarean birth, and glove change prior to skin closure, contribute towards reducing maternal morbidity and mortality.

KEYWORDS

current best practice, post-cesarean sepsis, prevention and treatment

1 | INTRODUCTION

Cesarean section (CS) is currently the most common major surgical procedure worldwide.¹ When medically indicated due to certain complications that arise during pregnancy or childbirth, it can be a life-saving procedure for both mothers and their newborns.² However, CS can lead to short- and long-term adverse health effects on women and their offspring.^{3–6}

The global cesarean birth rate has risen to 21.1% as of recent estimates, up from 7.1% in 1990.^{3–5} The increase in incidence has been highest in Eastern Asia, Western Asia, and North Africa, with the incidence being 44.9%, 34.7%, and 31.5% respectively.⁴ The highest incidences of cesarean births globally are 55.7% in Brazil, 60% in Cyprus, Turkey, and Romania, 72% in Egypt, and the highest rate seen in Greece at up to 75%. The global rate of CS is projected to be 28.5% by the end of 2030, resulting in a significant increase in infective morbidity and mortality globally if measures to mitigate complications related to CS are not strengthened.^{3,4} Numerous strategies exist to maintain cesarean birth rates at appropriate, evidence-based levels. One effective approach to reducing the risk of post-cesarean sepsis is avoiding cesarean births that are not medically indicated. This can be achieved by standardizing the definition and progress of labor, improved assessment and management of fetal heart rate tracings, offering external cephalic version for breech presentations, and finally a trial of labor for twin gestations when the first twin is in cephalic presentation.^{6,7} Another approach is to aim to increase the percentage of vaginal births after cesarean birth (VBAC), as this group has been shown to be a significant contributor to increasing cesarean rates.⁸

Infections accounted for 10.7% of maternal deaths globally in the period 2003–2009.⁹ During the period 2009–2020, pregnancy-related infection accounted for 7% of all maternal deaths,^{5–9} with a significant proportion occurring in the postpartum period.¹⁰

Results from the Multi-Country Global Maternal Sepsis Study (GLOSS), which included 2850 women from 52 countries, suggested that infections were the underlying cause of most hospital deaths attributable to either direct (e.g. abortion-related) and indirect (e.g. respiratory infection, meningitis) causes.¹¹ The GLOSS study also showed

that post-CS infections contributed to 60.6% of severe maternal outcomes in the study. The incidence of post-cesarean infection globally is in the range of 2.5%–20.5%.¹² Examples of infective morbidity may range from surgical site infection and endometritis to more significant complications, such as necrotizing fasciitis, pelvic abscess, septic pelvic thrombophlebitis, sepsis, and septic shock, which may lead to maternal mortality.¹³ Post-cesarean sepsis remains one of the major obstetric complications that is known to prolong hospital stays and result in additional surgery and maternal morbidity, leading to an increase in healthcare costs and socioeconomic consequences.³

1.1 | Contribution of CS to overall sepsis rates

The “Clean Care Is Safe Care” program by WHO demonstrates that surgical site infections (SSIs) form one third of the leading causes of hospital-related infections in low-income countries and the second leading cause in high-income countries.¹⁴ SSIs complicate 1.9% of all surgical procedures worldwide but the rate of post-cesarean infection is considerably higher at 7%–10%. Several low- and middle-income countries (LMICs) reported a high incidence of SSI post-cesarean section ranging from 9.7% in Vietnam, 10.9% in Tanzania, 16.2% in Nigeria, and 19.2% in Kenya compared to a lower rate of 2.9% in Europe. These studies, however, also revealed a great variability in the definition of SSI.¹⁵ The most common infections seen globally post-cesarean were SSIs seen in 2%–7%, endometritis in 2%–16%, and wound infections, such as necrotizing fasciitis, in 2%–16% of cases.¹⁵

1.2 | Defining sepsis

The Third International Consensus Definitions for Sepsis and Septic Shock Task Force in 2016 emphasized signs of organ dysfunction rather than signs of infection in defining sepsis and septic shock.¹⁶ The Task Force defined sepsis as a life-threatening organ dysfunction due to a dysregulated response to an infection. An increase of 2 or more points in the Sequential Organ Failure Assessment (SOFA) score is

considered organ dysfunction. There is increasing consensus that the definition of organ dysfunction should be based on specific criteria for the obstetric population over those used for SOFA and clinical markers preferred over laboratory investigations.¹⁷ Maternal sepsis has been comprehensively defined by WHO as “a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or postpartum period,” a definition that has been endorsed by the Surviving Sepsis Campaign and FIGO.¹⁸ The Global Maternal and Neonatal Sepsis Initiative was launched by WHO to “focus additional efforts, energize stakeholders and accelerate progress in the area of maternal and neonatal infection”.¹⁹

Delay in recognition of sepsis, antibiotic administration, and appropriate intensive monitoring and care can worsen the outcome and increase the risk of maternal death.^{20,21} Maternal sepsis needs to be recognized as an obstetric emergency.²¹ Recognizing risk factors and setting up of a care bundle to prevent sepsis and applying the principles of golden hour to maternal sepsis can contribute to reducing the incidence of this major complication.¹⁴

2 | PREVENTION OF POST CESAREAN SECTION SEPSIS

Identification of risk factors before and during surgery is the primary step towards prevention. These steps, along with strategies to promote infection control practices after CS can contribute towards reducing maternal and newborn sepsis.²¹ The risk factors responsible for post-CS sepsis are listed in Table 1.

2.1 | Preventing sepsis from cesarean section: Pre- and intraoperative

2.1.1 | Management of comorbidities

The presence of comorbidities like anemia, poorly controlled diabetes, and poor nutritional status are known to be associated

with increased incidence of postoperative infections.^{13,22,23} Adequate control of these can contribute to the prevention of post cesarean sepsis.

2.1.2 | Prophylactic antibiotic administration

A Cochrane Database systematic review by Smaill et al., which included 95 studies that evaluated the effect of antibiotic prophylaxis in over 15 000 women undergoing CS, found that the incidence of serious maternal sepsis was reduced by 70% and the rate of wound infection and endometritis was reduced by 60% after administration of prophylactic antibiotics versus no treatment or placebo, with no major maternal adverse outcomes.²⁴ The National Institute for Health and Care Excellence (NICE) guideline and WHO recommend administering the prophylactic dose of a single intravenous (IV) antibiotic before the skin incision.²⁵ WHO recommends that the dose of prophylactic antibiotic should be given 30–60 min before the skin incision, rather than after cord clamping or postoperatively, to reduce the incidence of maternal sepsis.²⁶ However, a recent Cochrane Database systematic review by Williams et al. concluded that further investigation and trials are needed to make firm recommendations regarding the appropriate timing of prophylactic antibiotics.²⁷

With regard to the choice of prophylactic antibiotics, a single dose of first-generation cephalosporins (e.g. cefazolin) or penicillin (ampicillin) is recommended over other classes of antibiotics, such as clindamycin plus gentamycin or clindamycin alone.^{13,24,26–28} Although reduction in SSIs is noted for all antibiotic subgroups without differences between subgroups for serious infections and wound infection, the largest reduction in endometritis is seen with natural penicillins. There is no evidence that multiple doses of prophylactic antibiotics significantly reduce the risk of febrile morbidity, wound infection, urinary tract infection, and length of hospital stay. However, multiple doses of prophylactic antibiotics significantly reduce the risk of endometritis (68% vs. 57%; $P=0.02$) compared to a single dose.^{29,30} Due to similar efficacy, increased healthcare costs, and risks of antimicrobial resistance,

TABLE 1 Risk factors for post-CS sepsis.^{13,22,23,33,54–57}

Host-related	Specific to pregnancy and intrapartum events	Surgical procedure related
Obesity (BMI >30)	Hypertensive disorder of pregnancy	Emergency CS
Rural population	Gestational diabetes mellitus	Non-use of prophylactic antibiotics
Maternal preoperative condition (ASA score 3)	Twin or greater order pregnancy	Uterine rupture
Pre-gestational diabetes mellitus	Preterm rupture of membranes	Cesarean hysterectomy
Previous CS	Prolonged rupture of membranes	Need for blood transfusion
Recurrent pregnancy loss	Prolonged labor especially second stage	Surgery duration >1 h
Severe anemia	Internal fetal monitoring devices	Large incision length
Bacterial vaginosis	Chorioamnionitis	Subcutaneous tissue thickness >3 cm
Group B <i>Streptococcus</i> colonization		Subcutaneous hematoma
Tobacco use		Excessive blood loss
Poor antenatal care		Second stage CS
Use of corticosteroids		
HIV patient with low CD4 count and high viral load		

Abbreviation: BMI, body mass index; CS, cesarean section.

multiple doses of prophylactic antibiotics should not be given routinely; however, additional doses may be considered in women with other clinical risk factors, such as surgical time longer than 2 h and excessive blood loss.³⁰ Antimicrobial prophylaxis should be limited to a maximum of three doses within 24 h.²⁹

A higher dose of prophylactic antibiotics can be considered for women with a body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) above 30.^{29,31} The addition of azithromycin in women undergoing cesarean delivery during labor or after rupture of membranes reduces the rate of endometritis and SSIs.³² The American College of Obstetrics and Gynecology (ACOG) recommends the use of clindamycin with an aminoglycoside for women with beta lactam allergy; however, the comparative efficacy results with cefazolin need further research.²⁸

2.1.3 | Shaving

Routine perineal or pubic hair shaving before birth as a means of preventing maternal peripartum infection is not recommended, as it has no clear beneficial effect.^{13,31,33}

2.1.4 | Routine preoperative cleansing of vagina

Vaginal preparation with an antiseptic solution prior to cesarean birth regardless of the existing risks for infection reduces the risk of postoperative endometritis.¹³ The WHO Maternal and Perinatal Health Guideline Development Group (MPH-GDG) recommended the use of an antiseptic to clean the vagina preoperatively for 30–60 s for all cesarean births. The antiseptic used may be povidone iodine or chlorhexidine gluconate with a non-alcohol-based preparation, to be done once immediately before the commencement of the surgery (e.g. after preoperative urinary catheterization) to prevent vaginal mucosal irritation and discomfort to the patient. Vaginal cleansing is considered an invasive procedure and repeated cleansing should be avoided.^{12,33}

2.1.5 | Cleaning of surgical site

Preparing the skin with chlorhexidine alcohol before cesarean birth reduces the incidence of postoperative wound infection compared to iodine-based alcohol preparations. However, there is no difference in the risk of endometritis and risk of adverse events. Hence, iodine preparations may be used when chlorhexidine preparations are not available.^{12,33}

2.1.6 | Skin incision type

A Cochrane review in 2013 reported that the incidence in postoperative febrile morbidity was reduced by 65% with the Joel Cohen Incision compared to the Pfannenstiel incision.³⁰ However, there

was no difference in SSI. The updated NICE guideline recommends considering a transverse incision made 3 cm above the pubic symphysis, with blunt dissection of the abdominal layers, as a more accurate description than the term “Joel Cohen incision,” for reducing operative and febrile morbidity during cesarean birth.²⁵ A recent randomized controlled trial comparing Joel Cohen and Pfannenstiel skin incisions for cesarean birth in women with a BMI of 35 or higher found that the Joel Cohen incision had no advantage over the Pfannenstiel incision and was instead associated with a higher composite adverse maternal outcome, although this did not achieve statistical significance.³⁴

2.1.7 | Glove changes

Changing gloves after delivery of the placenta, before closure of the abdominal wall, has been shown to reduce the incidence of SSIs. A recent systematic review and meta-analysis of a randomized controlled trial including 1948 women confirmed these findings.³⁵

2.2 | Other perioperative and intraoperative practices

Training the operating theater team in basic principles and repeated drills in aseptic techniques to be followed during elective and emergency CS births has been shown to reduce infection rates.¹³ No conclusive evidence has been found in the reduction of SSI with the use of perioperative oxygen supplementation.³⁶ There is no difference in wound-related morbidity when the depth of the subcutaneous tissue was <2 cm. In cases with a depth >2 cm, closure of the tissue resulted in a decrease in the complications associated with wound infection.^{13,30} Intra-abdominal saline irrigation was not associated with a reduction in infection.¹³ There is no significant difference in infection rate morbidity with sutures or skin staples used for wound closure for cesarean section.²²

A recent Cochrane Database systematic review on the use of negative pressure wound therapy (NPWT) for orthopedic, obstetric, vascular, and general procedures showed, with moderate certainty evidence, that it reduced the risk of SSI compared with standard dressing, reduced the incidence of mortality, and was cost-effective in obese pregnant patients undergoing cesarean section.³⁷

3 | CAUSES OF POST-CS SEPSIS

Sepsis following CS may be related to the surgical procedure, the pregnancy, or sepsis unrelated to the pregnancy or birth, as outlined in Table 2. Most postpartum sepsis is related to either genital tract or wound infections. Urinary tract infection is the most common cause of postnatal sepsis unrelated to the pregnancy, accounting for 12% of infections. Surgical injuries (such as bowel perforation) or complications related to regional anesthesia are a rare cause of post-cesarean sepsis.

TABLE 2 Causes of sepsis post-CS.^{17,21,38}

Cesarean-related	Pregnancy-related	Other causes of sepsis
• Wound infection • Necrotizing fasciitis • Bowel perforation • Meningitis/spinal abscess (related to regional anesthetic)	• Endometritis • Mastitis	• Urinary tract infection • Respiratory tract infection • Gastroenteritis • Infective endocarditis • Cholecystitis/cholangitis

Identifying a source of infection and causative organism is an important step in appropriately managing sepsis. In a UK population, a clinical source of infection was identified in 74% of cases, with a confirmed microbiological source found only in 64%.³⁸ This requires a thorough clinical assessment, including history assessing for any localizing symptoms and a comprehensive physical examination, followed by investigations as outlined below.

3.1 | Causative organisms

The most common causative organisms are *Escherichia coli*, *Streptococcus* species, and anaerobes, which together account for over 50% of cases of maternal sepsis and up to 60% of postpartum sepsis.^{23,38–40}

Group A beta-hemolytic *Streptococcus* (GAS), although less common, is an important organism to consider as infection is associated with increased risk of severe maternal morbidity, including streptococcal toxic shock syndrome and necrotizing fasciitis, intensive care admission, and maternal mortality.^{23,38,39} Most GAS infections occur in the postpartum period, due to ascending infection from the genital tract. GAS should be considered in all women who present with fever together with watery vaginal discharge or uterine tenderness postpartum.³⁸

Coliforms are associated with urinary sepsis and sepsis associated with preterm rupture of membranes and cervical cerclage. Anaerobic organisms are commonly associated with sepsis secondary to chorioamnionitis. Co-infection with both gram-positive and gram-negative infections is also common in chorioamnionitis.^{23,41}

Pregnant women are more prone to develop severe illness and sepsis after viral infections than non-pregnant women. Causative pathogens include influenza, varicella, herpes simplex virus, and COVID-19.²³

4 | RECOGNIZING SEPSIS

4.1 | Clinical features

Due to the significant morbidity and mortality associated with sepsis, and the importance of early detection, sepsis should be considered in all women who present with signs or symptoms of infection and clinical deterioration. Women should be reviewed daily in the postoperative period, including maternal vital signs, review of the surgical incision, and assessment for symptoms of

infection. Most cases of sepsis present after discharge from hospital; therefore, all women should be educated regarding symptoms that should prompt review, including fevers, purulent or malodorous lochia, severe lower abdominal pain or wound pain, or discharge.¹³

Early recognition of sepsis in the obstetric population can be challenging, as its typical clinical features may be altered by normal physiological changes in pregnancy. Normal pregnancy results in increased plasma volume, increased cardiac output, peripheral vasodilation, and tachypnoea, which may lead to over- or underdiagnosis of sepsis if non-obstetric reference ranges are used.^{17,42} This can be particularly difficult in the postpartum period, when rapid physiological adjustments lead to wide variation in the normal range for cardiorespiratory observations.^{21,43} Observations should always be recorded on maternity-specific charts. Recognizing sepsis requires a combination of the patient's medical history, physical examination, and an early warning score.

4.2 | Early warning systems

Several early warning tools have been developed to rapidly identify patients at risk of sepsis and prompt appropriate escalation of care (Table 3). Although no single screening tool has been shown to be superior at detecting sepsis, use of an early warning system can increase detection of sepsis and prediction of those at increased risk of severe morbidity and mortality. Early identification and escalation of care may reduce sepsis-related morbidity and mortality.^{21,44}

Most early warning systems were designed for use in a non-pregnant population and have not been validated in pregnancy and postpartum. Several scoring criteria have been modified, considering the physiological changes in normal pregnancy. A recent study evaluated 21 early warning systems and concluded that no single early warning system had sufficient specificity and sensitivity to accurately diagnose sepsis. However, obstetric-specific early warning systems performed better than non-obstetric-specific early warning systems in identifying women at risk of severe maternal outcomes.⁴⁵

Women with suspected infection should be assessed with an early warning system, as this may aid in the early detection and appropriate management of women at increased risk of adverse outcomes. Institutions should develop local protocols specific to the population and available resources.

TABLE 3 Pregnancy-specific early warning systems.^{17,58–60}

Early warning system	Criteria	Additional information
omqSOFA	- SBP <90 mmHg = 1 ≥90 = 0 - Respiratory rate ≥25 = 1 <25 = 0 - Altered mentation - Not alert = 1 - Alert = 0 If score ≥2, consider sepsis	Requires only clinical measures, so can be rapidly performed in any setting/resources
SOS	- Temperature - SBP - HR - RR - SpO₂ - WBC % Immature neutrophils - Lactate Each parameter scored 0–4^a Score ≥6, increased risk of ICU admission	- Requires clinical and biochemical data therefore may not be appropriate in all settings - Predictor of ICU admission - Score <6 has negative predictive value of 98.6%
California Maternal Quality Care Collaborative	- Temperature <36°C/>38°C (<96.8°F/>100.4°F) - HR >110 bpm for >15 min - RR >24 for >15 min - WBC >15 000/mm³ or <4000/mm³ If ≥2 of 4 criteria met: - Suspect serious infection - Commence initial action plan - Step 2: confirmation of sepsis (detailed sepsis evaluation) within 30 min	- Two-step screening process - Associated "action plan" at each stage of screening

Abbreviations: HR, heart rate; ICU, intensive care unit; omqSOFA, obstetric modified quick sequential organ failure assessment; RR, respiratory rate; SBP, systolic blood pressure; SOS, Sepsis in Obstetrics Score; SpO₂, oxygen saturation; WBC, white blood cell count.

^aScoring criteria for SOS: Temperature (°C): <30 = 4, 30–31.9 = 3, 32–33.9 = 2, 34–35.9 = 1, 36–38.4 = 0, 38.5–38.9 = 1, 39–40.9 = 3, >40.9 = 4; SBP (mmHg): >90 = 0, 70–90 = 2, <70 = 4; HR (bpm): <120 = 0, 120–129 = 1, 130–149 = 2, 150–179 = 3, >179 = 4; RR (bpm): <6 = 4, 6–9 = 2, 10–11 = 1, 12–24 = 0, 25–34 = 1, 35–49 = 3, >49 = 4; SpO₂ (%): <85 = 4, 85–89 = 3, 90–91 = 1, ≥92 = 0; WBC (10³/mm³): <1 = 4, 1–2.9 = 2, 3–5.6 = 1, 5.7–16.9 = 0, 17–24.9 = 1, 25–39.9 = 2, >39.9 = 4; % immature neutrophils: <10% = 0, ≥10% = 2; Lactate (mmol/L): <4 = 0, ≥4 = 2.

4.3 | Investigating sepsis

Once sepsis is suspected, investigations should be performed to determine the diagnosis, stratify risk, identify the source, and guide ongoing treatment. The initial investigation should include blood cultures (ideally two sets of cultures, each including aerobic and anaerobic bottles) before commencement of antibiotics. Maternal serum lactate is a marker for severity and can be used to monitor response to treatment. Additional investigations should be guided by clinical presentation, local patterns of disease, and local lab capabilities (Table 4). If early warning signs are positive, treatment should be initiated while awaiting results of investigations.

4.4 | Management of sepsis

4.4.1 | Sepsis care bundles

"Sepsis care bundles" have been developed to facilitate rapid evidence-based management of sepsis, and several have been developed in different patient populations (Table 5).

The components of care bundles vary depending on local procedures and resource viability, but all share the common principles of rapid assessment, early fluid resuscitation, and antibiotic treatment within the hour after identification of sepsis. Care bundles provide simplified pathways for clinicians to follow and can form the framework for education programs. When used consistently, care bundles have been associated with a reduction in mortality.

4.4.2 | Fluid resuscitation

Sepsis leads to fever, vasodilation, and capillary leakage, which causes hypotension and organ hypoperfusion. Restoration of circulating volume is essential to improve tissue perfusion and minimize end-organ dysfunction.

Initial fluid resuscitation should be commenced with 30 mL/kg of crystalloid, up to 2 L, within the first 3 h. An initial bolus of 500 mL should be given if there is hypotension, or an elevated serum lactate (>4 mmol/L).²³ There is no benefit associated with the use of albumin compared with crystalloid. Hydroxyethyl starch and gelatin have been associated with an increased risk of acute

TABLE 4 Investigations.^{17,21,23}

Investigations	Comments
Blood investigations	
- Serum lactate^a - Full blood count^a - Liver function tests^a - Creatinine, urea, electrolytes^a - Coagulation profile (PT/aPTT/INR, fibrinogen)^a	- Should be performed urgently – marker of severity ≥2mmol/L: senior review, IV fluids, repeat ≥4mmol/L: indicates high risk of deterioration, requires escalation of care - WBC >15 or <4 × 10³/mm³ or immature neutrophils ≥10% is a sign of severe sepsis - Platelet count <100 is a sign of severe sepsis - Derangement may suggest hepatic source of sepsis or may be a sign of organ dysfunction - Creatinine >90 - INR >1.5 or APTT >60s indicates severe sepsis
Microbiology	
- Blood cultures^a - Urine microscopy and culture^b - Vaginal swab^b - Wound swab^b - Stool culture^b - Culture vascular catheter lines^b	- Two sets of blood cultures (each including aerobic and anaerobic bottles) should be collected before commencing antibiotics - Samples for microscopy, culture, and sensitivities should be targeted to presenting signs and symptoms - May consider testing for <i>Clostridium difficile</i> if the patient had diarrhea and recent antibiotic treatment; however, this is an uncommon source of sepsis in obstetric patients
Virology	
Viral nasal/throat swab^b	- In setting where respiratory symptoms or findings are prominent - Guided by seasonal respiratory pathogens and lab capabilities
Biomarkers	
- C-reactive protein^b - Procalcitonin^b	- Non-specific inflammatory marker, elevated in bacterial sepsis. May be used to monitor treatment response - Can help to differentiate bacterial from viral sepsis in non-pregnant population. Results may be altered in pregnancy
Imaging	
- Chest X-ray^b - Pelvic ultrasound^b - CT^b - MRI^b	- Imaging should be performed if there are localizing symptoms or ongoing sepsis without identified source - Abdominal/pelvic imaging should be undertaken if there is suspicion of a postoperative collection - Percutaneous drainage may be performed concurrently if clinically appropriate

Abbreviations: APTT, activated partial thromboplastin time; CT, computed tomography; INR, International Normalized Ratio; IV, intravenous; MRI, magnetic resonance imaging; PT, prothrombin time; WBC, white blood cell count.

^aRoutine investigations: to be performed in all women with sepsis post-CS.

^bTargeted investigations: to be considered based on clinical suspicion of source.

TABLE 5 Care bundles.^{16,61,62}

Surviving sepsis	- Serum lactate - Blood cultures - Antibiotics - Fluids - Vasopressors if hypotensive after fluid resuscitation
UK sepsis trust "sepsis 6"	- Serum lactate - Bloods cultures - Antibiotics - Fluids - Oxygen - Monitor urine output
FAST-M (developed for use in low-resource settings)	- Fluids - Antibiotics - Source control - Transfer to higher-level care - Monitoring

kidney injury and therefore should not be used.⁴⁶ Caution should be taken in women with pre-eclampsia due to the risk of pulmonary edema.^{17,47}

Response to fluid resuscitation should be monitored with mean arterial pressure (MAP), serum lactate, capillary refill time, mental state, and urinary output. Other measures of fluid response include point-of-care ultrasound monitoring cardiac output, variation in pulse pressure, and variation in stroke volume.^{23,46,47} If there is inadequate response after 2 L of intravenous crystalloid, escalation of care is required.

4.4.3 | Antibiotic treatment

In suspected bacterial sepsis, administration of the appropriate treatment within the first hour significantly reduces the rate of mortality. A delay in antibiotic treatment in the general population has been shown to increase sepsis-related mortality by 8% per hour of delay.^{23,46,48} A UK population study of sepsis-related maternal mortality showed that of women who died from sepsis, only 33% received antibiotics within the first hour after diagnosis, and 58% within 3h.⁴⁹

Empiric broad-spectrum antibiotics should be commenced within 1 h of recognition of sepsis. Treatment should not be delayed

while awaiting results of investigations. Antibiotics should be tailored to the likely source and pathogens, and local patterns of resistance. Patients should be reassessed daily to monitor response to treatment and the need for ongoing intravenous antibiotic therapy. Once a pathogen is identified, treatment should be narrowed. Suggested empiric treatments are listed in Table 6; however, where available, local guidelines should be followed to reflect local patterns of resistance.

4.4.4 | Antimicrobial stewardship

Antimicrobial stewardship should be considered to minimize antibiotic resistance. Coverage should be narrowed as soon as a causative organism is identified; however, given that pregnancy-related or CS-related sepsis polymicrobial infections are likely, the antibiotic should properly cover anaerobes. There is limited guidance on the optimal duration of antibiotic treatment; however, evidence from the non-obstetric population indicates that shorter courses of antibiotics have similar efficacy to longer courses, but fewer side effects.²¹ Response to treatment should be assessed daily to determine the need for ongoing antibiotic therapy. All maternity services should work towards a lead for antibiotic stewardship alongside infectious diseases.

4.4.5 | Source control

Once a source of infection is identified, source control should be undertaken promptly. In a non-obstetric population, early source control within 6 h was associated with a reduced risk of 90-day mortality, with an adjusted odds ratio of 0.71.⁵⁰ This benefit was most pronounced in those with gastrointestinal or intra-abdominal sources of infection.⁵⁰

The goal of source control is to remove infected or necrotic tissue. In the post-cesarean population, source control may include drainage of pus or abscess—which may be performed percutaneously or

surgically—removal of infected devices (such as IV catheters), wound debridement, surgical removal of retained products of conception, or, rarely, hysterectomy.²³

Necrotizing fasciitis is an uncommon but life-threatening complication of cesarean birth, which is mostly caused by GAS but can be a non-specific polymicrobial infection. Necrotizing fasciitis should be suspected if there is pain out of proportion to the appearance of the wound. It can cause rapid deterioration and therefore early and aggressive surgical debridement should be undertaken if there is clinical suspicion.²³

Peripartum emergency hysterectomy may be performed as a life-saving procedure when it is the only means of source control in post-cesarean sepsis. It is considered by WHO as a “near-miss” for maternal mortality.⁵¹ A recent prospective cohort study of maternal sepsis globally showed that hysterectomy was performed in 1.9% of women admitted with maternal sepsis.¹¹ Due to the significant maternal physical and psychological sequelae, the decision for peripartum hysterectomy should ideally be made by a senior clinician after a multidisciplinary discussion.

4.4.6 | Escalation of care

If there is no response to initial resuscitation or further evidence clinical deterioration, care should be escalated to the intensive care unit.

Triggers for escalation of care should include:

- Cardiorespiratory compromise: persistent hypotension, circulatory instability, increasing supplemental oxygen requirement.
- Evidence of organ dysfunction: altered level of consciousness, oliguria, coagulopathy, hepatic dysfunction.
- Evidence of hypoperfusion: metabolic/lactic acidosis, clinical signs of poor tissue perfusion.
- No response to IV fluids: persistent elevated serum lactate or systolic blood pressure below 90 mmHg despite fluid resuscitation.^{17,52,53}

TABLE 6 Empiric antibiotics for maternal sepsis.¹⁷

	First-line treatment	Special considerations
Sepsis – unknown source (hospital-acquired)	• Piperacillin 4 g + tazobactam 0.5 g IV every 8 h • Consider gentamicin	Penicillin hypersensitivity: ciprofloxacin + vancomycin At risk of MRSA: add vancomycin At risk of multidrug-resistant gram-negative organism: meropenem (single agent)
Sepsis – unknown source (community-acquired)	• Amoxicillin/ampicillin 2 g IV every 6 h • Gentamicin 4–7 mg/kg IV • Metronidazole 500 mg IV every 12 h	Penicillin hypersensitivity (severe): clindamycin + metronidazole Penicillin hypersensitivity (mild–moderate): cephazolin + gentamycin + metronidazole
Wound infection	• Flucloxacillin 2 g IV every 6 h	Penicillin hypersensitivity (severe): vancomycin Penicillin hypersensitivity (mild): cefazolin At risk of MRSA: add vancomycin
At risk of GAS	• Add clindamycin 6000 mg IV every 8 h	Consider IV immunoglobulin ^a

Abbreviations: GAS, group A beta-hemolytic *Streptococcus*; IV, intravenous; MRSA, methicillin-resistant *Streptococcus aureus*.

^aIV immunoglobulin may neutralize circulating exotoxins in severe gram-positive necrotizing infections. Should be considered in critically ill patients only.



Post-Caesarean Sepsis

The Challenge

Maternal sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or in the postpartum period

Sepsis is the third most common direct cause of maternal mortality



Sepsis is a leading cause of complication post-caesarean section - the global incidence is 2.5 - 20.5%

Rates of caesarean section are rising globally. The current global rate of caesarean is 21.1%



Antenatal

Screen all women for risk factors for sepsis
Optimise management of comorbidities
Educate all women about symptoms of sepsis

Antenatal Risk factors

- Obesity
- Diabetes mellitus
- Severe anemia
- Smoking
- Steroid use
- Hypertensive disorders of pregnancy
- Multiple pregnancy

Intraoperative

Prophylactic antibiotics: a single dose of first-generation cephalosporins should be given routinely prior to skin incision.
Add azithromycin in caesareans during labour/after rupture of membranes.

Preparation: Clean skin with chlorhexidine alcohol.
Vaginal preparation prior to caesarean section.

Glove change: prior to closure of abdominal wall

Postnatal

Recognition

All women should be educated regarding symptoms of sepsis: fever, pain, abnormal discharge



All women with suspected infection should be assessed using an Early Warning System

Investigations: should include two sets of blood cultures, serum lactate, targeted microbiology testing, and imaging

Management

Early antibiotic treatment should be initiated within the first hour

Fluid resuscitation should be commenced immediately with 30mL/kg of crystalloid. Individualise care in women with preeclampsia or other comorbidities.



Source control should be undertaken as soon as possible

FIGURE 1 Overview of risk factors, prevention, and management of post-CS sepsis.

Intensive care management involves maintenance of volume status, cardiac output, and tissue perfusion. Vasopressors are used to maintain blood pressure and adequate tissue perfusion. Noradrenaline should be used as a first line in pregnancy, due to lower risk of arrhythmia and mortality compared with dopamine, and safety data from use to maintain blood pressure at the time of regional anesthetic. Inotropes are used to increase cardiac contractility and can be used in addition to noradrenaline to maintain adequate circulation. In patients with ongoing vasopressor requirements for at least 4h to maintain mean arterial systolic blood pressure, hydrocortisone is recommended due to the risk of sepsis-induced adrenal failure.^{52,53}

The response to treatment is monitored using invasive monitoring (e.g. arterial lines pulmonary artery catheterization) and non-invasive methods, such as serial transthoracic echocardiogram.

4.4.7 | Venous thromboembolism prophylaxis

Cesarean birth and sepsis are independent risk factors for venous thromboembolism.¹⁷ In women with post-CS sepsis, there is a high risk of venous thromboembolism, and pharmacological and mechanical prophylaxis should be commenced.

4.4.8 | Additional considerations

Sepsis may impact the initiation of lactation; therefore, ongoing breastfeeding support should be offered to all women according to their wishes. Most antibiotics are excreted in very small doses in breast milk and can safely be continued during breastfeeding; however, infants should be monitored for side effects, including gastrointestinal upset or thrush. Safety of specific agents should be considered.¹⁷ GAS has been reported to cause neonatal infection; therefore, in cases of maternal sepsis, the newborn should be assessed for early-onset neonatal sepsis.

Women who experience sepsis and other severe maternal morbidity are at increased risk of postpartum psychiatric conditions, including depression, anxiety, psychosis, and post-traumatic stress disorder. These typically present in the first 4 months postpartum. Adequate psychosocial support during treatment and long-term follow-up should be provided for all women with post-CS sepsis.⁵³

5 | SUMMARY

In conclusion, sepsis following CS is a severe, yet often preventable, complication characterized by the body's overwhelming response to

infection, which can rapidly progress to life-threatening organ dysfunction and requires rapid recognition, resuscitation, source control, and supportive care of the patient. Although SSIs site infections are a common precursor, sepsis can also stem from uterine infections, urinary tract infections, or other postpartum infections. Recognizing the early signs and symptoms, which can range from fever and rapid heartbeat to localized wound issues and foul-smelling discharge, is crucial for timely intervention. Most maternal deaths from sepsis occur in the postpartum period and this could be attributed to the immunological adaptations and further lends itself to prompt recognition with meticulous clinical examinations of the patient and use of early warning scores.

Understanding the various risk factors allows for targeted prevention strategies and increased vigilance in susceptible individuals. Untreated sepsis after CS can lead to devastating short- and long-term complications. However, with early diagnosis, aggressive antibiotic therapy, source control when necessary, and comprehensive supportive care, outcomes can be significantly improved. Emphasizing preventative measures, including prophylactic antibiotics and meticulous surgical techniques, alongside heightened awareness among patients and healthcare providers, remains paramount in minimizing the occurrence and impact of this serious condition, ultimately safeguarding maternal health and well-being (Figure 1).

AUTHOR CONTRIBUTIONS

EB proposed the idea for the guideline. FS, MLM, MM, DP, and EB worked on the concept for this practice guideline. DP, AL, and GK wrote the first draft of the manuscript. The remaining authors commented on the first draft. AL, GK, and EB edited and finalized the manuscript. AL and GK contributed equally to this work.

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Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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