



SEPSIS IN PREGNANCY: SOME OLD VERSES NEW INCLUSIONS

Obstetrics & Gynaecology

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ABSTRACT

Introduction: After having completed an uneventful pregnancy, some women remain healthy others suffer due to various disorders. Further in developing country like India, where malnutrition and anemia is rampant, women are more prone to get infected. There are chances of puerperal infection in the genital urinary tract and caesarean section, wound infection. Woman in post partum period are in need of greater awareness to prevent puerperal infection there by to prevent further problems in puerperal period.

Aim & Objective: Understand the common causes of sepsis and organisms involved in obstetrics and gynaecology. Recognise progression of infection towards severe sepsis and septic shock through available tools, such as the modified early obstetric warning systems (MEOWS), and instigate preventative measures. Staff Educational programmes to ensure 1) Avoidance of hand contamination and frequent use of alcohol gel 2) Use of personal protective equipment— gloves, disposable aprons, gowns, face mask and eye 3) Availability of infection control guidelines 4) Team training to follow guidance in emergency situations 5) Use of modified early warning scoring systems and education to enable early identification of septic patients

Methods of prevention : Staff Educational programmes to ensure 1) Avoidance of hand contamination and frequent use of alcohol el 32) Use of personal protective equipment— gloves, disposable aprons, gowns, face mask and eye protection 3) Availability of infection control guidelines 4) Team training to follow guidance in emergency situations 5) Use of modified early warning scoring systems and education to enable early identification of septic patients. Anaesthesia procedure and icu care carries most important role in survival.

CONCLUSION: The deaths from severe sepsis reported in the most two recent CMACE reports highlighted the insidious and subtle signs that were commonly unrecognized by the mother and the health professionals who attended her. Educating professionals, patients, and using a modified early obstetric warning scoring system may help in recognizing obstetric patients with early sepsis. The outcome in septic parturients may be improved by early provision of time-sensitive interventions such as adequate hydration, initiation of broad-spectrum antibiotics, eliminating the source of infection, and multidisciplinary team management. Further work is needed in defining diagnostic haemodynamic criteria that may be more clinically specific in a septic obstetric patient.

KEYWORDS

Sepsis, systemic inflammatory response syndrome (SIRS), Surviving sepsis guideline (SSG)

INTRODUCTION:

In the Saving Lives report 2014,⁵ the criteria taken from the UK Sepsis Trust differ in that the diagnosis can be made on single measurements of diagnostic criteria but have not been validated on pregnant women. Incidence and severity of these infections declined dramatically in the second part of the present century, for reasons including decreased virulence of the infecting organisms, in Sepsis and pregnancy. Sepsis and pregnancy. Sepsis is a common and potentially life-threatening condition caused by infection. Sepsis that occurs during pregnancy is called maternal sepsis. Sometimes called blood poisoning, sepsis is the body's inflammatory response to infection, but it can overload the body's ability to cope.

Understand the common causes of sepsis and organisms involved in obstetrics and gynaecology. Recognise progression of infection towards severe sepsis and septic shock through available tools, such as the modified early obstetric warning systems (MEOWS), and instigate preventative measures.

Sepsis in obstetric patients further complicates the diagnosis as alterations in physiology related to pregnancy can mask sepsis indicators normally seen in the general population. If early signs of sepsis go unrecognized, septic shock can develop, leading to organ dysfunction and potential death. Maternal early warning tools have been designed to assist clinicians in recognizing early indications of illness. Through use of clinical pathway- specific tools, disease processes may be detected early, subsequently benefiting patients with aggressive treatment management and intervention.

Definition

Sepsis: Sepsis is broadly understood to exist when an infectious process has triggered the systemic inflammatory response syndrome (SIRS). SIRS is an inflammatory response to physiological insult which is characterized by the presence of: The presence of two or more of the above signs describes SIRS.³

hyperthermia ($>38^{\circ}\text{C}$) or hypothermia ($<36^{\circ}\text{C}$), tachycardia (>90 beats min^{-1}), tachypnoea (>20 bpm) or $\text{PaCO}_2/\text{PaO}_2 <32$ mm Hg,

and leucophilia ($>12 \times 10^9$ litre $^{-1}$) or leukopenia ($<4 \times 10^9$ litre $^{-1}$).

The most difficult aspect of the recognition of SIRS in pregnancy is the differentiation of the condition from the normal physiological changes of pregnancy with which it overlaps. The criteria for the diagnosis have been suggested by UKOSS (as the presence of two or more of the following) but have not yet been validated.⁴

- Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$ measured on two occasions at least 4 h apart.
- Heart rate >100 beats min^{-1} measured on two occasions at least 4 h apart.
- Respiratory rate >20 bpm measured on two occasions at least 4 h apart.
- White cell count $>17 \times 10^9$ or $<4 \times 10^9$

litre $^{-1}$ or with $>10\%$ immature band forms, measured on two occasions. In the Saving Lives report 2014,⁵ the criteria taken from the UK Sepsis Trust differ in that the diagnosis can be made on single measurements of diagnostic criteria but have not been validated on pregnant women.

Severe sepsis

Severe sepsis is sepsis associated with organ dysfunction (hypotension, arterial hypoxaemia, lactic acidosis, renal failure, liver dysfunction, coagulation abnormalities, mental status changes). Septic shock

Septic shock is sepsis associated with hypotension despite i.v. fluid resuscitation leading to cell dysfunction and, if prolonged, cell death.

Puerperal sepsis

Puerperal sepsis is infection of the genital tract occurring at any time between rupture of membranes or labour and the 42nd day post-partum⁶ associated with two or more of the following: pelvic pain, fever, abnormal vaginal discharge, abnormal smell of discharge, or delay in reduction in the size of the uterus.

MICROBIOLOGY

The principle organisms identified were Group A Streptococcus, Streptococcus pneumoniae, Escherichia coli. In a small number of cases no organism was identified. Group A streptococcal puerperal sepsis (Group A streptococcus (β haemolytic S. pyogenes)) is a gram-positive coccus which grows in long chains or pairs. About 5–30% of the population are asymptomatic carriers and it is commensal in the skin and throat. It spreads easily by person-to-person contact or by droplet dispersion. The immune state of the host determines the presentation and ranges from no symptoms or mild respiratory, cutaneous, and soft tissue infections to serious invasive infections. Clinically, invasive group A streptococcus (GAS) infection has the potential to cause life-threatening conditions such as post-partum endometritis, streptococcal toxic shock syndrome, necrotizing fasciitis, and rapidly progressive septicemia and death.

In pregnancy, organisms may be transferred from throat or nose via hands to the perineum.

After delivery or membrane rupture, vaginal bacteria ascend into the uterus where blood and necrotic decidua provide excellent growth media for multiplication; causing mild non-specific inflammation.

Risk factors for infection

Otherwise healthy pregnant patients may have obstetric and non-pregnancy factors which increase the risk of sepsis (Table 1).

Table 1

Risk factors for sepsis
Obstetric factors
During pregnancy Amniocentesis
Cervical suture
During vaginal delivery
Prolonged rupture of membranes
Prolonged labour
Vaginal trauma

Surgical procedures Episiotomy Caesarean section Retained products
Non-obstetric factors Obesity Diabetes Immunosuppression Anaemia
Socioeconomic deprivation History of pelvic inflammatory disease
Black or other ethnic minority group

Overall, Caesarean section and obesity are the most common factors (CMACE), but it is important to remember other causes of sepsis or septic shock during pregnancy and puerperium as listed in Table 2.

Table-2

Causes of sepsis

Genital tract causes: chorioamnionitis, endometritis, septic abortion, wound infection after vaginal tear, episiotomy, or Caesarean section

Renal causes: lower urinary tract infection, pyelonephritis
Respiratory causes: pneumonia—bacterial, viral; tuberculosis

Intra-peritoneal causes: ruptured appendix, acute appendicitis, acute cholecystitis, bowel infarction Other causes: breast infection, septic pelvic thrombophlebitis, necrotizing fasciitis, malaria, miliary tuberculosis.

Role of anaesthetists and management of septic obstetric patients:

Obstetric anaesthetists use critical care skills as part of the team in the recognition, assessment, and management of septic obstetric patients; the role includes management of resuscitation, control of infection, providing anaesthesia for surgical intervention, transfer of patients to the imaging suite or intensive care, postoperative care, and also prevention.

Recognition of obstetric sepsis

As a consequence of altered physiology, signs and symptoms suggesting sepsis are less distinctive during pregnancy. For example, tachycardia is an early sign of sepsis, but basal heart rate is already raised as a result of physiological adaptation in obstetric patients.

In non-pregnant patients, sepsis presents as unregulated vasodilation leading to a state of relative hypovolaemia but in pregnancy, there is already vasodilation, caused by raised level of progesterone, and compensated by increased blood volume. The increased blood volume may mask cardiovascular signs in early sepsis.⁹ Sepsis-induced

anaerobic metabolism and lactic acidosis can cause profound tachypnoea, but an increase in respiratory rate may be potentially mistaken for the progesterone-induced hyperventilation of pregnancy.

Since the physiological parameters are less reliable, detailed history, and a high index of suspicion is paramount in the recognition of sepsis in pregnancy.

Clinical presentation varies depending on the source of infection, as summarized in Table 3.

Table 3

Clinical features

General symptoms: fever, rash, diarrhoea or vomiting, sore throat, shortness of breath, altered mental status, Specific symptoms: abdominal or pelvic pain or tenderness, vaginal discharge, premature contractions, sickle cell crisis, Signs: pyrexia ($>38^{\circ}\text{C}$), hypothermia (36°C), tachycardia (>100 beats min^{-1}), tachypnoea, arterial hypotension (SAP <90 mm Hg, MAP <70 mm Hg or SAP decrease >40 mm Hg in adults or <2 SD below normal for age), cool extremities, reduced capillary refill, acute oliguria, early pregnancy loss, fetal bradycardia, fetal tachycardia, intrauterine fetal death, Lab findings: leukocytosis, leukopenia, normal WBC with $>10\%$ immature forms, raised CRP, raised blood lactate, hyperglycaemia in the absence of diabetes, thrombocytopenia, coagulopathy, raised creatinine, hypoxaemia (Pa O₂/Pa O₂/FIO₂ <300), hyperbilirubinaemia The CMACE report¹ has particularly identified the presence of tachypnoea, neutropenia, and hypothermia as the most ominous signs.

Diarrhoea is a common symptom of pelvic sepsis and the combination of abdominal pain and abnormal or absent fetal heart rate may signify sepsis rather than placental abruption.

The raised white cell count (WCC) of pregnancy decreases after delivery, but a WCC that fails to reach normal levels or decreases rapidly may indicate severe infection.^{1,9}

Resuscitation and management

The aim of management is to maintain oxygenation and perfusion of vital organs and placenta while identifying and treating infection. Survival has been shown to be improved by using the Surviving Sepsis campaign guidance^{9,10} and administered in the first hour of diagnosis.¹¹

Sepsis bundles (as mentioned in Table 4) are a group of interventions designed to allow the team to follow the timing, sequence, and goals of individual elements of care to improve the outcome.¹²

Table 4

Sepsis bundles

Within 1 h, the 'Sepsis Six' has to be followed:

Administer high-flow oxygen

Take blood cultures both aerobic and anaerobic without delay. At least two sets of blood culture should be obtained, one drawn percutaneously and one from a vascular site, unless the device was recently inserted

Administer broad-spectrum antibiotics

Fluid resuscitation—administer 20 ml kg^{-1} crystalloid for hypotension or if lactate ≥ 4 mmol litre⁻¹

Measure serum lactate

Catheterize and measure accurate hourly urine output Within 6 h: Administer vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain MAP ≥ 65 mm Hg

In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ 4 mmol litre⁻¹, measure CVP and ScvO₂/ScvO₂ and maintain CVP 8–12 mm Hg, ScvO₂/ScvO₂ 70% and mixed venous saturation 65% Serial measurement of lactate if initial lactate was elevated

The Key message from 'Saving Lives, Improving Care 2014' is 'Timely recognition, Fast administration of intravenous antibiotics and Quick involvement of experts—senior review is essential'. Other recommendations for management: The pregnant woman should be managed in the left lateral position to avoid aortocaval compression. Samples for baseline blood tests such as full blood count, coagulation profile, renal function

tests, and C-reactive protein should also be sent at presentation.

- i. **Fluids:** perform crystalloid fluid challenge until there is haemodynamic improvement based on central venous pressure (CVP)- directed sepsis goals.
Obstetric patients at term have a greatly increased fluid volume, may have preeclampsia, or be receiving uterotonic drugs that lead to fluid retention. They are at risk of developing pulmonary oedema and non-invasive cardiac output monitoring should be considered to guide fluid resuscitation.¹¹
- ii. **Vasopressors And Ionotropes:** norepinephrine is the first choice as a vasopressor to maintain mean arterial pressure (MAP) ≥ 65 mm Hg. If MAP is not achievable, epinephrine can be added. Vasopressin is not recommended as an initial agent, but can be added later to reduce the dosage of norepinephrine. In the presence of myocardial dysfunction or ongoing signs of hypoperfusion despite achieving adequate intravascular volume and MAP, dobutamine should be administered.
- iii. **Corticosteroids Should Be Avoided:** may be considered if haemodynamic instability continues despite resuscitation.
- iv. In the absence of ischaemic heart disease or signs of hypoperfusion, it is suggested to maintain haemoglobin at 70–90 g litre⁻¹.
- v. **Sepsis is associated with coagulopathy:** monitoring and correction of coagulopathy is required.
- vi. **Early advice form an infectious disease physician or microbiologist should be sought:** this is essential in instances where the woman fails to respond to the first choice antibiotic. Other samples guided by clinical suspicion of the focus of infection (throat swabs, midstream urine, high vaginal swab, wound swab, breast milk, stool, epidural site or CSF, swabs from baby) should also be obtained ideally before starting antibiotic therapy. If the MRSA status is unknown, a premoistened nose swab should be sent for screening.

Control of infection

Controlling the source of infection is paramount and it may require both medical and surgical intervention.

Antibiotics should be administered in the first hour of recognition; delay is associated with a worse outcome. The doses of antibiotics in pregnancy are unchanged. Early involvement of a microbiologist is strongly recommended.

The following is the recommended i.v. antibiotic therapy by CMACE. Antifungals are not needed empirically in sepsis and these drugs should be avoided in pregnancy and lactation unless potential benefits outweigh the risk.

- i. When the patient is not critically ill, coamoxiclav or cefuroxime or cefotaxime and metronidazole; in penicillin allergic cases, clarithromycin or clindamycin and gentamicin.
- ii. When the patient is septic, piperacillin– tazobactam or meropenem or ciprofloxacin and gentamicin. Metronidazole may be considered for anaerobic cover.
- iii. For group A streptococcal infection, clindamycin is more effective than penicillin.
- iv. For MRSA cover, consider teicoplanin or linezolid.

Once antibiotic and haemodynamic therapies have been started, any potential surgical source of infection should be established.

After detailed physical examination and satisfactory stabilization, radiological investigations (ultrasound scan, CT, and MRI of the abdomen and pelvis) should be considered and revisited if there is an inadequate response to therapy or the clinical presentation suggests intra-abdominal pathology.

A surgical focus of infection as listed in Table 5 should be drained promptly.¹³

Table-5

Surgical procedures in sepsis management
Evacuation of retained products of conception
Debridement of wound infection or fasciitis
Percutaneous drainage of abscesses

Stent or percutaneous nephrostomy for obstructive pyelonephritis
Delivery of fetus if chorioamnionitis is suspected

Hysterectomy for myometrial necrosis

If chorioamnionitis is suspected as the most likely cause of sepsis, early delivery of fetus should be considered. In extreme cases, hysterectomy may need to be considered if myometrial necrosis is the source of infection.

Non-obstetric sources of infection should be borne in mind and include appendicitis, pancreatic abscesses, or infarcted bowel.

The culture and bacterial sensitivities of an infected tissue should be performed to guide antibiotic therapy.

Anaesthesia For Surgical Intervention

The decision of delivering the fetus or continuing the pregnancy is influenced by patient's condition, gestational age, fetal status, presence of chorioamnionitis, and labour.

The well-being of the fetus is compromised if sepsis reduces maternal AP and placental perfusion, whereas the gravid uterus beyond 20 weeks may cause decrease in lung volumes and venous return.

Maternal sepsis may induce both labour and fetal death. Occasionally, if the risks of continuing pregnancy outweigh the benefits of delivery, administration of antenatal steroids should be considered to improve the outcome of a premature fetus.

The decision process should involve a obstetrician, neonatologist, microbiologist, intensivist, anaesthetist, and patient is essential.

If surgical intervention is needed, the anaesthetists are required to make the decision on regional or general anaesthesia.

Regional anaesthesia

Neuraxial block, which is a safety standard in obstetrics, is usually contraindicated in septic patients because: However, as with all clinical judgements, the decision to perform the surgery under regional or general anaesthesia must be considered on a case-by-case basis, assessing the risk–benefit ratio.

Septic vasodilated hypotensive patients may not tolerate the sympathetic block associated with spinal anaesthesia.

There may be associated coagulopathy or thrombocytopenia.

There is a risk of epidural abscess or meningitis; which is very small in patients treated with antibiotics as evidenced by isolated case reports and small studies.

General anaesthesia

General anaesthesia is highly likely to be required in a septic parturient. The principles of general anaesthesia in an obstetric patient should be followed and in the patient with haemodynamic instability, ketamine may be considered for induction of anaesthesia.

Intra AP, CVP, and cardiac output monitoring are helpful, especially for the postoperative phase.

The oxytocin bolus should be administered using an infusion pump over 5 min to avoid haemodynamic instability.¹⁴

The decision to extubate or transfer to critical care is influenced by severity of sepsis and an appreciation of the altered physiology of pregnancy.

After operation, oxygen is recommended to meet the increased demand.

Analgesia should be maintained with paracetamol and opioids. Non-steroidal anti-inflammatory drugs are contraindicated because septic patients have deranged renal function and coagulation profile and they may mask the presentation of invasive streptococcal infection, leading to delay in intervention. Postoperative care and transfer to critical care
After surgery, high dependency unit care is needed for continuous close observations of vital parameters. If the patient is critically ill with features of severe sepsis as mentioned in Table 6, transfer to critical care is needed for mechanical ventilation, vasopressor support, or haemofiltration.

Table 6

Indications for transfer to critical care unit

Respiratory: Airway protection, pulmonary oedema, ARDS

Cardiovascular: Persistent hypotension or raised serum lactate despite fluid resuscitation

Renal:

Acute renal failure Neurological ,Decreased conscious level Miscellaneous, Multiorgan failure.Documentation, communication and lessons learnt at all stages of management, effective communication among team members and good documentation is vital. It has also been recommended that a high quality multidisciplinary serious incident/root cause analysis should be carried out on all maternal deaths and all women with severe sepsis by the unit in which the women was cared for².

Prevention

As health professionals, education for ourselves and for our patients of the most basic aspects of hygiene and disease is needed to reduce the morbidity and mortality from severe maternal sepsis.

Early warning scores are extensively and effectively used in acute settings for early identification of critically ill patients. The physiological changes of pregnancy render these scoring systems inappropriate for obstetric patients. Although maternity hospitals have introduced a modified early obstetric warning scoring system, there is not yet a nationally agreed system in the UK.

Early recognition of sepsis.

Routine vaginal swab culture from pregnant women should be considered and the presence of GAS should be treated promptly before delivery to avoid a potentially lethal situation.¹⁶

In an obstetric patient undergoing Caesarean section, preoperative measures can reduce the risk of wound infection. The measures include abstaining from smoking (30 days) before surgery, glycaemic control in diabetics, treating any existing infection before elective section, showering with an antiseptic agent the night before surgery, hair removal by clippers, vaginalcleansing, and antimicrobial prophylaxis.¹⁷ In addition to prophylactic antibiotic at induction in a Caesarean delivery, further doses after 4h in prolonged surgical cases or those associated with excessive blood loss should be considered.¹⁸

Wide ranging and comprehensive measures are required to prevent and monitor infection as mentioned in Table 7.

Table 7
Measures For Prevention

Staff Educational Programmes To Ensure

- 1) Avoidance of hand contamination and frequent use of alcohol gel
- 2) Use of personal protective equipment- gloves, disposable aprons, gowns, face mask and eye protection
- 3) Availability of infection control guidelines
- 4) Team training to follow guidance in emergency situations
- 5) Use of modified early warning scoring systems and education to enable early identification of septic patients

CONCLUSION

The deaths from severe sepsis reported in the most two recent CMACE reports highlighted the insidious and subtle signs that were commonly unrecognized by the mother and the health professionals who attended her. Educating professionals, patients, and using a modified early obstetric warning scoring system may help in recognizing obstetric patients with early sepsis. The outcome in septic parturients may be improved by early provision of time-sensitive interventions such as adequate hydration, initiation of broad-spectrum antibiotics, eliminating the source of infection, and multidisciplinary team management. Further work is needed in defining diagnostic haemodynamic criteria that may be more clinically specific in a septic obstetric patient.

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