

SEPSIS AND SEPTIC SHOCK IN PREGNANCY AND PUERPERIUM

Dra Mariona Generó, Dra Patricia Ferrer, Dra M^a Dolores Gomez-Roig

1. INTRODUCTION

Maternal sepsis is a rare syndrome in high-income countries, with a reported incidence of between 0.1-0.3%, particularly the postpartum period being the riskier. Nonetheless, sepsis accounts for up to 10% of the maternal deaths and 15% of maternal admissions to the intensive care unit (ICU).

The most recent definition of sepsis and septic shock, for the general population, is found in the latest International Consensus presented in 2016 (Sepsis-3) from the SCCM/ESICM. These criteria may overestimate or underestimate the diagnosis in pregnant women, given the physiological changes that occur during pregnancy and the puerperium. Therefore, there are some modified scores to increase the sensitivity and specificity in the detection of sepsis, such as the obstetric q-SOFA (quick-Sequential [Sepsis-Related] Organ Failure Assessment), which is a bedside tool helps to quickly identify patients at high risk of sepsis using only clinical information.

Early identification and appropriate management in the initial hours of the infected obstetric patient who may go on to develop sepsis is imperative, since it will be the main prognostic factor in the evolution of these patients.

2. DEFINITIONS

SEPSIS

Life-threatening organ dysfunction caused by a dysregulated host response to infection. Sepsis remains a leading cause of maternal mortality in approximately 10% of the general population.

This new definition involves the search for a new clinical tool that replaces the systemic inflammatory response syndrome (SIRS) criteria in the identification of patients with sepsis, since these criteria are not present in all patients with infection, and they necessarily reflect an abnormal response on the host that conditions a threat to survival. In the latest update, the terms systemic inflammatory response syndrome (SIRS) and severe sepsis were abandoned in favour of simply using the categories infection, sepsis and septic shock.

SEPTIC SHOCK

A subset of sepsis with profound circulatory, cellular and metabolic abnormalities substantially increase mortality. Clinically, this includes patients who, despite adequate fluid resuscitation, require vasopressor support to maintain a mean arterial blood pressure ≥ 65 mmHg and have a serum lactate ≥ 2 mmol/L (18 mg/dl). This situation reflects mortality rates above 40%.

3. AETIOLOGY

The cause of infection in gestational and puerperal sepsis may have a pelvic or non-pelvic origin. *Table 1* shows the most frequent causes of sepsis. During the antepartum period, the most frequent causes of sepsis are non-pelvic, while intrapartum and postpartum causes are usually of pelvic origin (chorioamnionitis, endometritis). In 30% of cases the focus is not identified.

Mastitis are frequent infections that are not usually complicated, although the systemic response can be significant.

| Antepartum | Postpartum |
|--|---|
| <ul style="list-style-type: none"> • Urinary tract infections • Pneumonia • Appendicitis • Septic abortion • Chorioamnionitis | <ul style="list-style-type: none"> • Endometritis • Wound infection • Urinary tract infection • Pneumonia • Gastrointestinal |

Table 1. Sepsis causes.

The most frequently isolated organism in cases of maternal sepsis is *Escherichia coli* and group A and B streptococcal, although *Staphylococcus*, gram-negative, anaerobic bacteria, and many other organisms have also been identified.

Polymicrobial infections are more frequent in pregnant women than in the general population. In 15% of deaths due to maternal sepsis, in which the microbiological cause has been identified, they were polymicrobial infections. These findings support the recommendation to start broad-spectrum antibiotics until the pathogens are identified. In cases of typically polymicrobial infections (such as peritonitis), the possibility of polymicrobial infection is considered even if there is a single microorganism identified or we have negative cultures.

| Infection | Microorganism |
|-------------------|---|
| Common bacteria | <ul style="list-style-type: none"> - Group A- Beta haemolytic <i>Streptococcus (GAS) pyogenes</i> - <i>Escherichia coli</i> - Group B- <i>Streptococcus</i> - <i>Klebsiella pneumoniae</i> - <i>Staphylococcus aureus</i> - <i>Streptococcus pneumoniae</i> - <i>Proteus mirabilis</i> - Anaerobic microorganisms |
| Uncommon bacteria | <ul style="list-style-type: none"> - <i>Haemophilus influenzae</i> - <i>Listeria monocytogenes</i> - <i>Clostridium</i> species - <i>Mycobacterium tuberculosis</i> |
| Virus | <ul style="list-style-type: none"> - Influenza - Varicella zoster virus - Herpes simplex virus - Cytomegalovirus - SARS-CoV2 |

Table 2. Infectious causes of sepsis in pregnancy and postpartum

4. DIAGNOSIS

Physiological changes in pregnant women condition changes in the normal ranges of clinical and analytical parameters. The normal physiological changes of pregnancy may mask early signs of sepsis. Additionally, other pre-existing comorbidities (LES, coagulation disorders) or pregnancy pathologies (autoimmune thrombocytopenia, preeclampsia, gestational hypertension) can affect the baseline situation of the patient and they should be taken into account at the time of evaluation.

| Parameters | Changes compared to general population |
|--------------------------|--|
| Temperature | Unmodified |
| Systolic blood pressure | Unmodified |
| Diastolic blood pressure | Decreased 5-10 mmHg in the second trimester |
| Heart rate | Varies between 83 ±10 bpm, being normal until 100 bpm |
| Respiratory rate | Unmodified |
| Oxygen saturation | Unmodified |
| Leukocytes | Considered normal between 5.700-16.900, and intrapartum until 30.000 |
| Neutrophils | Unmodified |
| Lactic acid | Unknown |
| Central Venous Pressure | 1 st trim: 6.5 - 8.2 cmH ₂ O |
| | 2 nd trim: 3.6 - 4.6 cmH ₂ O |
| | 3 rd trim: 2.0 - 4.4 cmH ₂ O |

Table 3. Changes in clinical and analytical parameters in pregnant women

4.1 SEPSIS

Suspected sepsis

In the presence of a patient with suspected infection, the q-SOFA score is applied. If it is a pregnant-puerperal patient, the obstetric q-SOFA score should be applied, modified to increase sensitivity (from 37.5% to 81.2%) and specificity (from 72.2% to 75%) in pregnant patients.

The q-SOFA score is a rapid method with a high negative predictive value for sepsis. A baseline score of 0 is considered unless the patient is known to have had organ dysfunction prior to the onset of infection. We will suspect sepsis when at least 2 criteria are present.

- None or 1 criterion: Low suspicion of sepsis. Clinical monitoring and reassessment.
- 2 or more criteria: High suspicion of sepsis. Apply the SOFA scale (Table 5).

A q-SOFA score ≥ 2 reflects an overall mortality risk of approximately 10% in the general population.

| Variables | Punctuation | |
|-------------------------|--------------------|--------------------|
| | 0 | 1 |
| Systolic blood pressure | ≥90 mmHg | <90 mmHg |
| Respiratory rate | <25 breaths/minute | ≥25 breaths/minute |
| Altered mental status | Alert | Not alert |

Table 4. Obstetrically modified q-SOFA score.

Diagnosis of sepsis

Organ dysfunction is defined as an acute change in SOFA score as a consequence of infection.

The diagnosis of sepsis is confirmed when a score > or equal to 2 is obtained on the SOFA scale:

| Variables | Punctuation | | |
|--|-------------|-------------------|----------------------|
| | 0 | 1 | 2 |
| Respiration PaO ₂ /FiO ₂ | ≥ 400 | 400-300 | <300 |
| Coagulation (Platelets x 10 ⁶ /L) | ≥150 | 150-100 | <100 |
| Liver (Bilirubin μmol/L) | ≤20 | 20-32 | >32 |
| Cardiovascular (Mean arterial pressure) | MAP ≥70 | MAP <70 | Require vasopressors |
| Neurological | Alert | Rousable by voice | Rousable by pain |
| Renal (Creatinine μmol/L) | ≤90 | 90-120 | >120 |

Table 5. Obstetrically modified SOFA score (Sepsis-related Organ Failure Assessment)

FiO₂: fraction of inspired oxygen (expressed as a decimal); MAP: mean arterial pressure; PaO₂: partial pressure of oxygen (in mmHg).

4.2 SEPTIC SHOCK

It is defined as a situation in which the underlying circulatory, cellular, and metabolic abnormalities are profound enough to substantially increase mortality.

Sepsis with the presence of both criteria despite correct hydro-electrolyte replacement:

SEPSIS



- Persistent hypotension requiring vasopressor therapy to maintain a mean arterial pressure ≥ 65 mmHg despite adequate fluid resuscitation
- Serum lactate ≥ 2 mmol/L (18 mg/dl) after adequate fluid resuscitation

5. INITIAL INVESTIGATIONS

The following complementary tests should be requested in a patient with suspected sepsis.

- Complete blood count, liver and renal function test (with bilirubin), coagulation studies, Plasma C-reactive protein.
- Venous blood gases analysis
- Serum lactate
Does not increase predictive validity but may help to identify intermediate risk. It is useful to guide resuscitation, achieving normalisation of lactate in cases of hypoperfusion. Serial monitoring is used to follow the therapeutic response and it is a prognostic tool in patients with sepsis and septic shock regardless the presence of hypotension and/or hypoperfusion.
- Procalcitonin

It is a useful biomarker to support the decision to start, de-escalate or even interrupt antibiotic treatment safely (but never as a single criterion). It may indicate the patients with the worst prognosis in terms of mortality.

- Blood cultures

They should be extracted even if the patient does not have fever and before antimicrobial therapy. Two blood cultures will be extracted in an aerobic and anaerobic media if possible before administration of antibiotics. Two different extractions will be made (one for each culture) from the catheter and/or from peripheral blood. Their collection should not delay antibiotic treatment. It is important to specify in the request if they have been extracted from peripheral blood or from a catheter (as well as the identification of the catheter) to facilitate the interpretation of the results.
- Urine culture

Spontaneous urination is better than urinary catheter. Once again, it is important to make different requests for microbiology and inform if it is postpartum to facilitate the interpretation of the results.
- Microbiological cultures from suspected sources

If an intrauterine origin is suspected in pregnant women: amniotic fluid culture (by amniocentesis), vaginal, rectal and endocervical swap. Evaluate stool culture if abundant diarrhoeas (Salmonella, Campylobacter, other parasites). If one has puerperal fever asses an endometrial culture.
- If chest pain: request ECG and Troponin
- Fetal assessment – CTG and/or fetal ultrasound

Imaging tests

The performance of imaging tests will be assessed according to the suspected site of infection according to clinical- analytical evolution. As an example:

- Renal ultrasound in case of suspected urinary focus.
- Gynaecological ultrasound in case of suspicion of endometritis with retained placenta.
- Chest radiography in case of suspected pneumonia or acute pulmonary oedema.
- Abdominal and pelvic CT if abdominal collection, intestinal or urological lesion, or septic pelvic thrombosis is suspected.
- Head CT or MRI if altered level of consciousness.
- In any shocked patient without an apparent focus, an imaging test should be performed (abdominal ultrasound, CT, etc.) to rule out a renal and biliary focus and assess whether there is obstruction of the pathways.

6. MANAGEMENT AND TREATMENT (See Figure 1- Algorithm 1-)

Once a presumed diagnosis of sepsis or septic shock has been made, after obtaining the cultures, antimicrobial therapy will start as soon as possible, ideally before the first hour ('golden hour'). Among patients with sepsis and septic shock, survival decreases 7% for every hour of delay in antibiotics administration.

Symptomatic treatment will also be indicated as soon as possible, within the first 3 hours, with the intention of improving the haemodynamic status and tissue perfusion.

6.1 INITIAL RESUSCITATIVE THERAPY

In the emergency department, or from the moment of diagnosis, basic monitoring will be performed: blood pressure, heart rate, temperature, respiratory rate, fluid balance, O₂ saturation, and glycemia. The patient should remain under observation and consider the management according to the first reassessment at 2h.

- If organic disease is ruled out and the patient remains haemodynamically stable, she will be admitted to the high-risk hospitalisation. Broad-spectrum antibiotic treatment will be started during the first hour and analytical control will be requested at 6-12h (including complete blood count + hepatorenal profile (with bilirubin) + acid-base balance + coagulation tests + PCR + lactate + procalcitonin). Vital signs monitoring every 4 hours, or sooner if worsening.
- If there is a high suspicion of sepsis, or signs of organic dysfunction are evident, the patient will be admitted to the Intermediate Obstetric Care Unit (UCOI) for strict monitoring of signs and early initiation of antibiotic and symptomatic treatment. Once at UCOI, her management will be carried out jointly with the Anaesthesiology Service, deciding the type of monitoring necessary (permanent urinary catheterisation, fluid balance, need for central or peripheral venous access, etc.). Clinical reassessment will be performed at 2 hours and analytical reassessment at 6-12 hours.

6.2 ANTIBIOTIC THERAPY

Antibiotic therapy should be started as soon as possible (within the first hour after diagnosis), after performing cultures, provided that collection does not delay administration.

- If the focus is known, start empirical broad-spectrum antibiotic treatment according to the specific condition (see corresponding protocol). If it is available, adjust according to antibiogram.
- In case of focus compatible with abscess/collection, assess drainage in the first 12 hours.
- In the case of sepsis of unknown source, previous antibiotic treatment (in the last three months) or prolonged treatment, no response to treatment after 48 hours or a patient in septic shock: **MEROPENEM** 1-2 g/6-8h (administer the first dose in 30 minutes and the following in 4 hours) + **DAPTOMYCIN** (10 mg/kg with a maximum dose of 700 mg. There are 500 mg and 350 mg vials) or **LINEZOLID** 600 mg/12 ev
If allergic to penicillin: **AZTREONAM** 1-2 g/6-8h (administer the first dose in 30 minutes and the following ones in 3-4 hours) + **AMIKACIN*** 1 g/24h (to be evaluated in patients with renal insufficiency) IV or **FOSFOMYCIN*** 2 g/6h (Assess the Na⁺ overload that can occur in patients with hypertension/preeclampsia, heart failure or ascites. It requires adjustment in renal failure) + **DAPTOMYCIN** (10 mg/kg with a maximum dose of 700 mg. There are 500 mg and 350 mg vials) or **LINEZOLID** 600 mg/12 ev.

***Amikacin and Fosfomycin** are the two options we have to cover ESBL in pregnant patients allergic to penicillin.

Tigecycline is classified as category D during pregnancy (alterations in fetal bone development) although it is classified as low risk during lactation. Its low oral bioavailability means that its ability to pass into infant plasma from ingested breast milk is null or negligible, EXCEPT in premature infants and the immediate neonatal period, in which there may be greater intestinal absorption. For this reason, in the postpartum period, the regimen in patients allergic to penicillin can be modified by **TIGECYCLINE** 200 mg for the first dose followed by 100 mg/12h + **DAPTOMYCIN** (10 mg/kg with a maximum dose of 700 mg. There are 500 mg and 350 mg vials) or **LINEZOLID** 600 mg/12 ev.

Review antibiotic treatment in the first 3-5 days. As soon as the aetiology of the infection is known, the antibiotic treatment must be adjusted to indicate the optimal therapy. The evaluation of the aetiology of the infection (interpretation of the microbiological results) must be carried out, evaluating the pathogen and antibiotic susceptibility and/or proper clinical improvement.

The possibility that a positive culture in non-sterile samples is the result of colonisation or contamination must be considered, as well as the polymicrobial aetiology in cases of infections that are typically polymicrobial, even though only one pathogen has been found in the cultures.

Apart from these considerations, treatment should be adjusted to the microbiological results obtained, suspending unnecessary antibiotics and using those with as narrow a spectrum as possible, promoting sequential therapy with the transition from intravenous to oral antibiotic treatment.

In patients with severe sepsis or septic shock without clinically relevant microbiological results, antibiotic de-escalation can be considered based on the clinical evolution and the decrease in biomarkers.

6.3 SYMPTOMATIC TREATMENT

6.3.1 INTRAVENOUS FLUIDS

Fluid resuscitation will be the first step in haemodynamic support for patients with hypotension and/or hypoperfusion (fever, vasodilation, and capillary refill lead to inadequate preload in patients with sepsis). Fluid therapy must be carefully developed, avoiding overhydration, and always adapted to the clinical situation and comorbidity of the patient (oliguria, O₂ saturation <95%, etc.), since pregnant patients have an increased risk of developing acute pulmonary oedema.

In **puerperal** women, an initial bolus of **30 mL/kg** of crystalloids (physiological saline/Ringer's lactate) is recommended for the first 3 hours and in **pregnant** women starting the administration with **20 mL/kg** of crystalloids is reasonable, adapting the dosage according to the clinical response of the patient.

It is estimated that 50% of patients who are hypotensive due to sepsis respond to fluid therapy; for the rest, excessively aggressive administration of fluids can lead to the creation of a 3rd space, diastolic ventricular dysfunction, and increased mortality.

Oral intake will not be contraindicated if there is no need for surgery in the next few hours (once the patient has been correctly resuscitated and is in a stable situation).

6.3.2 OXYGEN THERAPY

Oxygen therapy will be started if oxygen saturation (O₂) is less than 93% in puerperal women or 95% in pregnant women, with the aim of achieving an O₂ saturation of between 96-98%, reducing tachypnoea and a respiratory rate < 22 rpm. This action will be agreed with the anaesthesia team.

Initially, oxygen therapy will be administered with nasal prongs or ventimask with FiO₂ 28-35%, switching to high flow, if necessary, with FiO₂ 50-100%. If tachypnoea > 30 rpm and/or PaFi < 200 (PaFiO₂ = PaO₂/FiO₂) persists, it is an indication for mechanical ventilation and admission to the ICU.

6.3.3 VASOPRESSORS

They will be indicated according to the evolution of the patient's haemodynamic status and agreed with the Anaesthesiology Service.

In hypotensive patients who do not respond to fluid therapy or are not candidates for intensive resuscitation (due to acute pulmonary oedema or another contraindication), vasopressors can be used to increase blood pressure (reverse systemic vasodilatation and maintain adequate organ perfusion).

Norepinephrine is the first-line agent over the vasopressor during pregnancy and postpartum in sepsis with hypotension that does not respond to fluid resuscitation, with the aim of maintaining a MAP (mean arterial pressure) equal to or > 65 mmHg (individualise according to the patient and their particularities). Dosage of Norepinephrine ev. 0.5 µg/Kg/min.

If the patient persists with arterial hypotension (MAP < 65 mmHg) or presents myocardial dysfunction, treatment with inotropes is useful, as Dobutamine. Dobutamine ev. 2.5 - 10 µg/Kg/min.

6.4 OTHER MEASURES

- **Thromboembolic prophylaxis** (LMWH, low molecular weight heparin): venous thromboembolism prophylaxis will be recommended if there is no suspicion of acute bleeding or indication of termination of pregnancy or surgery in the next few hours. Remember the dose adjustment if renal involvement. If there is a contraindication for heparin, physical compression measures of the lower limbs will be performed (see specific protocol).
- **Anaemia treatment/prophylaxis**: red blood cell transfusion will be indicated if haemoglobin < 7 g/dL to achieve levels between at least 7 and 9 g/dL (once tissue hypoperfusion has resolved). Assessment of a patient's overall clinical status and consideration of extenuating circumstances such as myocardial ischemia, severe hypoxemia, acute haemorrhage or ischemic arterial disease. If there is no need for transfusion, iron supplementation will be indicated.
- **Treatment of thrombocytopenia**: in patients with severe sepsis or septic shock, in the absence of apparent bleeding, it is suggested that platelets be administered preventively when counts are ≤ 10,000/mm³; as well as when the counts are ≤ 20,000/mm³ if the patient presents a significant risk of bleeding. Higher platelet counts (≥ 50,000/mm³) are recommended in cases of active bleeding, surgery, or invasive procedures.
- **Glycaemic control**: blood glucose monitoring will be intensified (BMTtest every 1-2 hours until blood glucose levels are stable and every 4 hours thereafter). Hyperglycaemia can be found in patients without a history of diabetes, which should be treated, preferably with rapid insulin, if glycemia > 180 mg/dL in two consecutive determinations.

Regular insulin regimen (according to BMTtest):

- 60-160: 0 IU
- 161-200: 4 IU
- 201-240: +1 IU
- 241-280: +2 IU
- 281-320: +3 IU
- 321-350: +4 IU
- >350: ev infusion

Treatment adjustment in diabetic patients (gestational and pre-pregnancy) will be assessed, given the increased risk of ketoacidosis in the context of sepsis.

- **Stress ulcer prophylaxis**: gastric protection to prevent subsequent upper gastrointestinal bleeding: Pantoprazole 40 mg/24h ev.

7. ICU CRITERIA

Together with the Anaesthesiology team, the need to transfer the patient to the Intensive Care Unit (ICU) will be assessed when one of the following criteria is met:

| ICU admission criteria: 1 major or 3 minors | |
|--|--|
| MAJOR CRITERIA | |
| <ul style="list-style-type: none"> • Need for invasive mechanical ventilation/pulmonary oedema • Shock without initial response to treatment with vasopressors • Persistent hyperlactatemia despite fluid therapy (>2 mmol/L or >18 mg/dL) • Multi-organ failure • Acute renal failure/oliguria/need for renal clearance techniques • Altered mental status despite correct oxygen and fluid therapy • No clinical improvement 3-6 hours after starting treatment | |
| MINOR CRITERIA | |
| <ul style="list-style-type: none"> • Respiratory rate > 30 rpm • PaO₂/FiO₂ < 250 • Multilobar infiltrates • Confusion/disorientation/altered mental status • Uraemia (BUN>20 mg/dL) • Leukopenia < 4,000 cells/mm³ • Thrombocytopenia <100,000 cells/mm³ • Hypothermia/Central BP < 36°C • Hypotension requiring administration of aggressive fluids | |

Table 9. Indications for involvement of ICU

8. FETAL MANAGEMENT AND MONITORING

- **Intrauterine sepsis:** as chorioamnionitis (see corresponding protocol), delivery should always be considered regardless of the gestation.
- **Extrauterine sepsis:** the case will be evaluated on an individual basis, taking into account the gestational age, the severity of the maternal condition, its evolution and the mode of delivery. Termination of pregnancy during maternal instability can increase maternal and fetal mortality. Therefore, maternal stabilisation will be prioritised, unless there is suspicion of loss of fetal well-being.
- We will perform NST (Non stress test) if gestational age >28 weeks (every 24h). If alterations are detected in the NST, assess the haemodynamic status of the pregnant woman, since it may be an indicator of maternal hypoxemia/acidosis.
- If delivery is considered, the administration of **Betamethasone** for fetal lung maturation and **magnesium sulphate** for fetal neuroprotection should be indicated depending on the gestational age (see corresponding protocols).
- The **mode of delivery** will be assessed individually based on the balance of risks/benefits of the vaginal and abdominal routes.
- **Epidural/intradural** anaesthesia should be avoided in the context of sepsis, although it can be individually assessed taking into account the risk/benefit of regional analgesia, anaesthetic alternatives, and the risk of central nervous system infection.

9. SPECIAL SITUATIONS

➤ **Toxic shock from Group A Streptococcus (pyogenes) (GAS) and Staphylococcus aureus**

This is an infrequent situation, but given the risk of toxic shock, if the patient has a bacteraemia by these Gram-Positive germs, we will contact:

- Infectious Diseases Service.
- Paediatric Service to assess prophylaxis in the newborn, given the risk of neonatal sepsis in patients who are breastfeeding and have GAS infection.

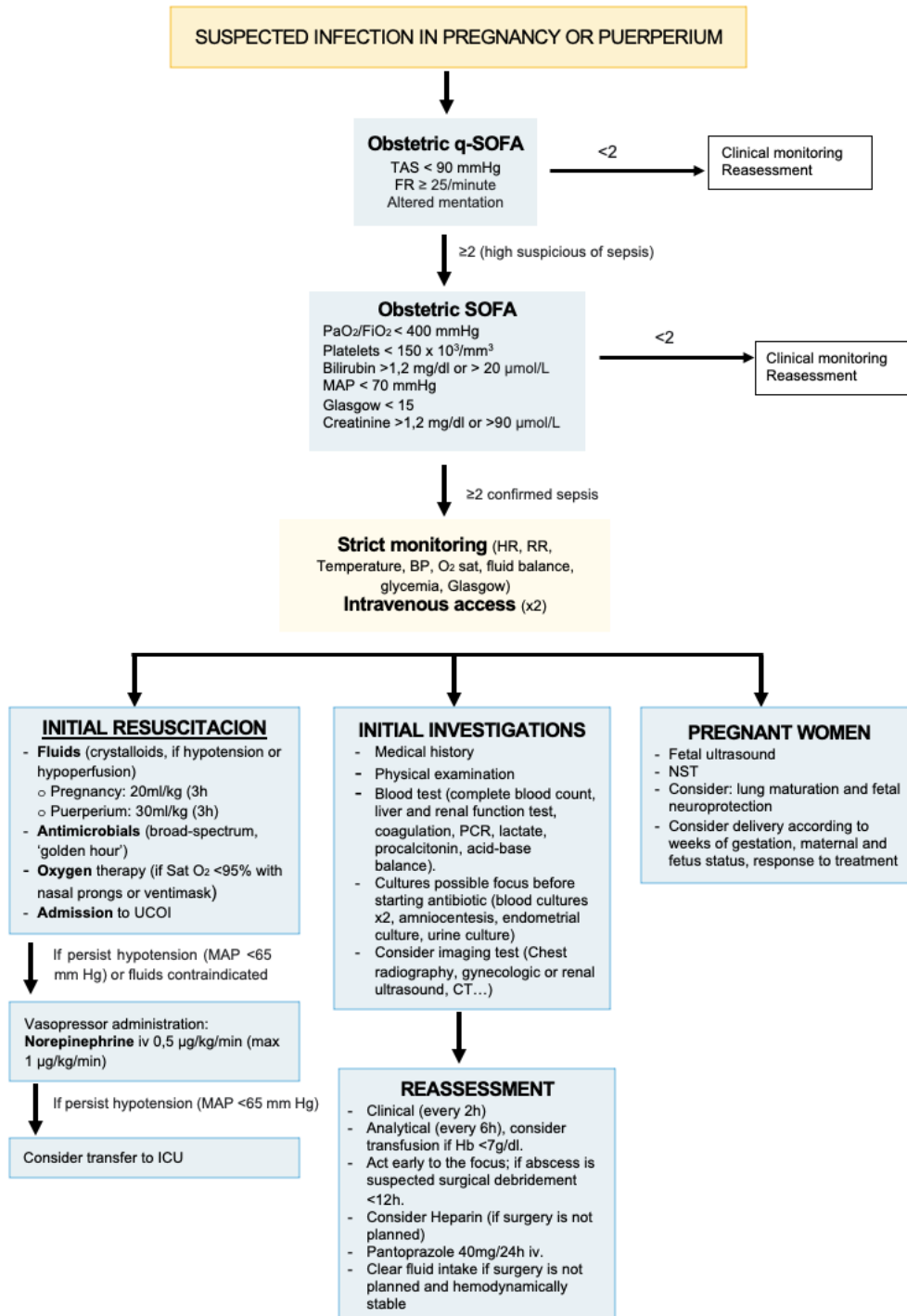
Contact isolation of the patient will be carried out in a single room, to avoid contagion, and hygienic and protection measures will be applied to visitors and health personnel (mask, gown, gloves).

➤ **Post treatment diarrhoea**

In the presence of persistent diarrhoea after aggressive antibiotic treatment (especially if beta-lactams), assess the possibility of Clostridium difficile infection by detecting toxins in faeces. Culture will also be requested if other bacterial (Salmonella, Campylobacter) or parasitic infections are suspected, mainly in patients with a history of recent travel abroad.

SUPPLEMENTARY DATA

ALGORITHM 1: ASSESSMENT AND MANAGEMENT OF SEPSIS IN PREGNANCY



SUSPECTED INFECTION IN PREGNANCY OR PUERPERIUM

Obstetric q-SOFA
 SBP < 90 mmHg
 RR ≥ 25/minute
 Altered mental status

<2 → Clinical monitoring
Reassessment

≥2 (high suspicious of sepsis)

Obstetric SOFA
 PaO₂/FiO₂ < 400 mmHg
 Platelets < 150 x 10³/mm³
 Bilirubin >1.2 mg/dl or > 20 μmol/L
 MAP < 70 mmHg
 Glasgow < 15
 Creatinine >1.2 mg/dl or >90 μmol/L

<2 → Clinical monitoring
Reassessment

≥2 confirmed sepsis

Strict monitoring (HR, RR, Temperature, BP, O₂ sat, fluid balance, glycemia, Glasgow)
Intravenous access (x2)

INITIAL RESUSCITATION

- **Fluids** (crystalloids, if hypotension or hypoperfusion)
 - o Pregnancy: 20 ml/kg (3h)
 - o Puerperium: 30 ml/kg (3h)
- **Antimicrobials** (broad-spectrum, 'golden hour')
- **Oxygen** therapy (if O₂sat < 95% with nasal prongs or ventimask)
- **Admission** to UCOI

If persist hypotension (MAP < 65 mm Hg) or fluids contraindicated

Vasopressor administration:
Norepinephrine ev 0.5 μg/kg/min (max 1 μg/kg/min)

If persist hypotension (MAP < 65 mm Hg)

Consider transfer to ICU

INITIAL INVESTIGATIONS

- Medical history
- Physical examination
- Blood test (complete blood count, liver and renal function test, coagulation, PCR, lactate, procalcitonin, acid-base balance).
- Obtain cultures of possible focuses of infection (blood cultures x2, amniocentesis, endometrial culture, urine culture)
- Consider imaging test (Chest radiography, gynecologic or renal ultrasound, CT, etc.)

PREGNANT WOMEN

- Fetal ultrasound
- NST
- Consider: lung maturation and fetal neuroprotection
- Consider delivery according to weeks of gestation, maternal and fetus status, response to treatment

REASSESSMENT

- Clinical (every 2h)
- Analytical (every 6h), consider transfusion if Hb <7g/dl.
- Act early to the focus; if abscess is suspected surgical debridement <12h.
- Consider Heparin (if surgery is not planned)
- Pantoprazole 40 mg/24h ev.
- Clear fluid intake if surgery is not planned and hemodynamically stable

BP: blood pressure; CT: computed tomography; FiO₂: fraction of inspired oxygen; Hb: haemoglobin; HR: heart rate; ICU: intensive care unit, iv: intravenous; MAP: mean arterial pressure; NST: non stress test; O₂ sat: oxygen saturation; PaO₂: partial pressure of oxygen (in mmHg), PCR: Plasma C-reactive protein; RR: respiratory rate; SBP: systolic blood pressure; UCOI: Intermediate Obstetric Care Unit