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Sepsis and pregnancy: do we know how to treat this situation?

Sepse e gravidez: sabemos tratar?

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ABSTRACT

Sepsis is defined as an acute inflammatory response syndrome secondary to an infectious focus. It has a high incidence, morbidity and mortality, causing substantial financial costs, especially due to complications such as septic shock and multiple organ dysfunction. The pathogen toxins associated with individual susceptibility culminate with cytokine release, which promotes a systemic inflammatory response that can progress to multiple organ dysfunction and eventual patient death.

Specifically, sepsis incidence, morbidity and mortality are lower in pregnant women, as this group is typically younger with fewer comorbidities having a polymicrobial etiology resulting in sepsis.

Pregnant women exhibit physiological characteristics that may confer specific clinical presentation and laboratory patterns during the sepsis course. Thus, a better understanding of these changes is critical for better identification and management of these patients. The presence of a fetus also requires unique approaches in a pregnant woman with sepsis.

Sepsis treatment is based on certain guidelines that were established after major clinical trials, which, unfortunately, all classified pregnancy as a exclusion criteria.

Thus, the treatment of sepsis in the general population has been extrapolated to the pregnant population, with the following main goals: maintenance of tissue perfusion with fluid replacement and vasoactive drugs (initial resuscitation), adequate oxygenation, control of the infection source and an early start of antibiotic therapy, corticosteroid infusion and blood transfusion when properly indicated, prophylaxis, and specifically monitoring and maintenance of fetal heath.

Keywords: Sepsis; Pregnancy; Pregnancy complications, infectious

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INTRODUCTION

The relevance of sepsis is becoming more noteworthy worldwide, as its incidence is progressively increasing due to several factors. Among these factors are the following: increasing life expectancy, a greater number of associated comorbidities, invasive procedures, transplanted and/or immunosuppressed individuals, and an increased prevalence of bacterial resistance.[1,2] The incidence of sepsis is estimated to be increasing at a rate of 9% annually.[3] Sepsis represents the main cause of mortality in intensive care units (ICUs), with an annual cost of 17 billion USD.[1,4]

A review published in 1998,[5] comprising 10.694 patients, found a sepsis-related mortality rate of 49.7%, with a declining trend across the

investigated period. Brazilian data[6] indicate that 30.5, 17.4 and 14.7% of admissions to the ICU were due to sepsis, severe sepsis and septic shock, respectively. The mortality indices were 33.9, 46.9 and 52.2%, respectively.

The situation of sepsis during pregnancy is quite different, as it is a rare occurrence. In addition one study found a decline from 0.6% in 1979 to 0.3% in 2000.[3] However, recent results indicate an increase of sepsis-related maternal mortality from 0.85 deaths/100,000 pregnant women in 2003-2005 to 1.13/100,000 in 2006-2008,[7] which is concerning.

That increase in the number of cases and severity of sepsis among the obstetric population is due to the large number of women who become pregnant after the age of 40 years and presented with high rates of comorbidities such as obesity, type 2 diabetes and systemic arterial hypertension.[8] Moreover, new technologies used for insemination and fetal medicine increase the prevalence of high-risk pregnancies.

Although septic shock is an even more rare occurrence after delivery (0.002 to 0.01%), it represents one of the main causes of admission of pregnant women to the ICU. According to the World Health Organization, sepsis is one of the four main causes of pregnancy-related mortality worldwide, together with hemorrhage, hypertensive disease and abortion.[9]

Because of the regional distribution of the causes of maternal mortality, the cases due to sepsis vary from 2.1 to 11.6%.[9] In countries with poor socioeconomic conditions, the infectious causes exert a crucial impact on maternal mortality.[10] However, because of the poor data record in those countries, the reported rates of maternal mortality by sepsis are not fully reliable and might be underestimated.[11]

Although the mortality of pregnant women with septic shock is lower compared with the overall population, its rate is a cause of concern, as it varies from 0 to 3% and up to 20 to 50%.[11]

The lower mortality rate exhibited by the obstetric population is due to the presence of protective factors, including a lower frequency of comorbidities and a younger age, while the source of infection is usually easy to locate, thus facilitating diagnosis and consequent surgical treatment, when it is indicated.[11-14]

It is worth emphasizing some possible complications of sepsis during pregnancy such as increased rates of premature births, fetal infection, hypoxia and acidosis, higher fetal mortality and increased probability to be necessary to perform cesarean.[15]

The aim of the present narrative review was to describe the main particularities of sepsis during pregnancy. It addition, it aims to alert intensivist doctors and gynecologists to the challenges posed by the diagnosis and treatment of this severe clinical condition that also affects pregnant women.

The search was initially conducted in the PubMed database using the keywords ("MESH words") "critical illness" OR "intensive care" OR "critical care" OR "intensive care unit" AND "pregnancy", which resulted in 9.926 articles. A second search was conducted using keywords ("MESH words") "pregnancy" AND "sepsis" OR "severe sepsis" OR "sepsis syndrome", which resulted in 129.330 articles. As the number of articles was too large, the results of the two searches were mutually crossed, reducing the number of articles to 436, which served as our reference base.

As pregnancy is a universal criterion of exclusion in studies on the septic syndrome, resulting in limited and scarce evidence for this group, we decided to perform a narrative review on the subject of interest. Although narrative reviews do not fit the model for systematic reviews, their relevance is nonetheless significant. Moreover, the latest review on the subject of interest published in Portuguese dates to 2008,[16] which indicates the need for a recent review including the latest studies on sepsis.

DEFINITION

During a consensus conference conducted by the Society of Critical Care Medicine in 1992,[17] the systemic inflammatory response syndrome (SIRS) was defined as a disseminated organic inflammatory response to various types of insult characterized by the presence of at least two of the following criteria: fever or hypothermia (body temperature >38ºC or <36ºC), tachycardia (heart rate >90bpm), tachypnea (respiratory rate >20 breaths per minute or arterial carbon dioxide tension - $PaCO_2$ <32mmHg), and leukocytosis or leukopenia (white blood cell count >12,000/mm^3 or <4,000/mm^3 or >10% of immature forms). In turn, sepsis was defined as SIRS associated with the presence of an infection source. However, those definitions were established based on non-pregnant individuals.

Another conference conducted in 2001[18] attempted to improve the sepsis definition (Table 1) by establishing criteria with sufficient sensitivity to allow for a rapid suspicion of sepsis at the bedside, thus allowing for early diagnostic investigation and immediate onset of treatment.

Table 1 - The diagnostic criteria for sepsis in the presence of confirmed or suspected infection

General	Core temperature >38.3ºC or <36ºC Heart rate >90bpm or >2 SD above the normal value for age Tachypnea Altered mental status Significant edema or positive fluid balance (>20ml/kg over 24 hours) Hyperglycemia (plasma glucose >110mg/dL or 7.7mmol/L)
Inflammatory	White blood cell count >12,000/μL or <4,000/μL Normal white blood cell count with >10% immature forms Plasma C reactive protein >2 SD above the normal value Plasma procalcitonin >2 SD above the normal value
Hemodynamic	Systolic blood pressure <90mmHg, mean arterial pressure <70 or a systolic blood pressure decrease >40mmHg in adults or <2 SD below normal for age $ScvO_2$ >70% Cardiac index >3,5L/min/m^2
Organ dysfunction	PaO_2/FiO_2 <300 Urine output <0.5mL/kg/h Creatinine increase ≥0.5mg/dL INR >1.5 or APTT >60s Platelet count <100,000/μL Ileus (absent bowel sounds) Plasma total bilirubin >4mg/dL or >70mmol/L
Tissue perfusion	Lactate >3mmol/L Decreased capillary refill or mottling

SD - standard deviation; $ScvO_2$ - central venous oxygen saturation; PaO_2 - arterial oxygen partial pressure; FiO_2 General - fraction of inspired oxygen; INR - international normalized ratio; APTT - activated partial thromboplastin time.

In addition, the normal values on laboratory tests in obstetric women differ from the overall population.[19] For instance, serum creatinine levels >1.0mg/dL are considered abnormal for the obstetric population, who exhibits several other differential characteristics such as pregnancy-induced leukocytosis, tachypnea with consequent metabolic alkalosis and increased heart rate that make early recognition of sepsis difficult, as indicated in table 2.

Table 2 - The physiological changes in pregnancy and their impact on diagnosis

System	Changes	Impact
Cardiovascular	↓ peripheral vascular resistance ↑ heart rate ↓ arterial pressure ↑ cardiac output	Masking of initial signs of sepsis Increased hypoperfusion
Blood	↑ plasma volume ↑ red cell volume Anemia	Greater reduction of oxygen supply to tissues
Respiratory	↑ tidal volume ↓ residual volume ↑ minute-ventilation by 30-40% ↑ respiratory center simulation → ↑ respiratory rate ↓ da $PaCO_2$	Delayed physiological response to metabolic alkalosis Impaired oxygenation
Renal	Ureteropelvic dilation and ↓ureteral pressure due to smooth muscle relaxation Flaccid bladder ↑ intravesical pressure due to the pregnant uterus weight ↑ vesicoureteral reflux ↑ renal plasma flow ↑ glomerular filtration rate ↓ urea and creatinine average values Asymptomatic bacteriuria	Delayed identification of renal injury secondary to sepsis Favorable to pyelonephritis
Gastrointestinal	↓ muscle tone across the digestive tract Delayed gastric emptying Diaphragm elevation by the pregnant womb Changes in bile composition ↑ production of pro-inflammatory cytokines bye Kupffer cells	↑ risk of bacterial translocation ↑ risk of aspiration pneumonia ↑ risk of cholestasis, hyperbilirumbinemia and jaundice
Coagulation	↑ factors VII, VIII, IX, X, XII, Von Willebrand and fibrinogen ↓ protein S ↓ fibrinolytic activity	↑ risk of thrombotic events ↑ risk of DIC
Genital	↓ vaginal pH ↑ glycogen in vaginal epithelium	↑ risk of chorioamnionitis

$PaCO_2$ - arterial carbon dioxide partial pressure; DIC – disseminated intravascular coagulation.

PATHOPHYSIOLOGY

Certain physiological changes that occur during pregnancy deserve particular attention,[20] as they may hinde an early sepsis diagnosis, reduce the physiological response to the triggering factor, and facilitate certain particular types of infection (Table 2).[11,16,20,21]

Sepsis involves an exacerbated systemic inflammatory response against an infectious stimulus, which varies as a function of the host's age, the presence or absence of comorbidities, nutritional status, the virulence of the infectious agent, and the source of infection.

As a result of the stimulus represented by the infecting agent toxins, the body defense cells release large amounts of pro-inflammatory cytokines, which activate the endothelial tissue resulting in the production of various SIRS effectors and a wide range of systemic changes.[22-26] The final result of that process is an imbalance between oxygen supply and consumption, which is followed by generalized tissue hypoperfusion, cell hypoxia, anaerobic metabolism, hyperlactatemia, and acidemia that culminate in multiple organ dysfunction syndrome (MODS).

The severity of the clinical presentation of sepsis and its prognosis depends on the intensity of SIRS and its clinical repercussion in the various organic systems and can be assessed using scores such as Sequential Organ Failure Assessment (SOFA).[27]

However, no such score has yet been validated for the obstetric population, which makes their prognosis prediction difficult.[28]

As the fetal immune system is not completely formed, fetuses exhibit decreased SIRS in response to infectious stimuli, as shown in animal studies.[29,30]

ETIOLOGY AND PREDISPOSING FACTORS

In the obstetric population, the urogenital tract represents the most frequent source of infection leading to sepsis. Thus, most cases of sepsis in that population are caused by Gram-negative bacteria[31] and exhibit a greater tendency toward polymicrobial sepsis (anaerobic bacteria, Gram-positive bacteria, and fungi are potentially present in the urogenital flora). In immunosuppressed women, as is the case of human immunodeficiency virus (HIV) carriers, diabetic individuals, and women who use corticosteroids, sepsis might be caused by opportunistic agents.

Tables 3 and 4 indicate the main causal agents and the main diagnoses associated with septic shock in pregnant women, respectively.[32]

Several predisposing factors for sepsis during pregnancy have been described, among which, cesarean sections, lack of prenatal care, lack of policies for legal abortion, induction of abortion, and premature rupture of membranes stand out. Moreover, the following factors should be considered: conditions inherent to the obstetric population such as the presence of aerobic and anaerobic bacteria in the vagina and endocervical canal,

Table 3 - The microbial causes of septic shock in pregnant women

Gram-negative	*Escherichia coli* *Hemophilus influenzae* *Klebisiella*species *Enterobacter* species *Proteus*species *Pseudomonas* species *Serratia*species
Gram-positive	*Pneumococcus* *Streptococcus*, groups A, B, and D *Enterococus* *Staphylococcus aureus* *Listeria monocytogenes*
Anaerobic	*Bacteroides* species *Clostridium perfringens* *Fusobacterium* species *Peptococcus* *Peptostreptococcus*
Fungi	—

Table 4 - The main diagnoses associated with severe infection in obstetric patients

Infections associated with pregnancy and/or pregnancy-related surgical procedures	Chorioamnionitis Postpartum endometritis Septic abortion Septic thrombophlebitis Puerperal sepsis Infection of cesarean section wound Episiotomy infection Necrotizing fasciitis Pelvic abscess Infected cerclage Amniocentesis - septic abortion Umbilical cord biopsy
Infections unrelated to pregnancy but occurring more often in the obstetric population	Lower urinary tract infection Pyelonephritis Malaria Listeriosis Viral hepatitis (E) Varicella pneumonia Coccidioidomycosis Aspiration pneumonia
Incidental infections during pregnancy	Community-acquired pneumonia HIV-related infections Toxoplasmosis Cytomegalovirus Gastrointestinal infections Disseminated herpes
Hospital-acquired infections at any hospital site including the ICU	Pneumonia nosocomial Ventilator-associated pneumonia Catheter-related urinary tract infection Central line-associated infection Skin and soft tissue infection related to peripheral intravenous catheters; infected surgical wound

HIV - human immunodeficiency virus; ICU – intensive care unit.

bacterial propagation during vaginal delivery, possible infection of the surgical site in cesarean sections and episiotomies, multiple genital examinations during the peripartum period, and reduction of the cell-mediated immune response.[33,34]

TREATMENT

Sepsis treatment must be initiated as soon as possible to improve patient prognosis and reduce mortality. Implementation of quick-response staff members for the identification and initial treatment of individuals with sepsis increases their survival odds.[35,36]

The base treatment, which also applies to pregnant women with sepsis, is provided by the therapeutic guidelines based on the Surviving Sepsis Campaign[37] together with specific measures aimed at the prevention of infection after surgical procedures.[38] Nevertheless, it is worth mentioning that the obstetric population was not specifically considered when establishing the guidelines.

In the obstetric context, the assessment of fetal vitality has particular relevance, as the balance between fetal oxygen supply and consumption might be severely altered in the presence of maternal sepsis. Maternal stabilization by focusing on definite targets appears to represent the best approach to ensure fetal vitality.

Initial approach and early hemodynamic resuscitation

The initial management of sepsis must be directed by an institutional protocol that includes parameters for the early detection of individuals with sepsis, who should then be preferentially admitted to the ICU.

Treatment should be initiated immediately and should be aimed to restoring adequate levels of tissue perfusion as established by the early goal-directed therapy (EGDT) criteria:[39] central venous pressure (CVP) equal to 8 to 12 mmHg, mean arterial pressure (MAP) ≥65mmHg, urine output ≥0.5mL/kg/h, and central venous oxygen saturation ($ScvO_2$) ≥70% or mixed venous oxygen saturation (SvO_2) ≥65%.

Initial fluid infusion should be performed with 30mL/kg of crystalloids, which should be repeated as needed to achieve the goal of $ScvO_2$ ≥70%. Nevertheless, fluid overload should be avoided, especially after the first six hours.[40]

Importantly, EGDT does not take pregnant women into consideration, and there are no reports in the literature on the positive impact of its application to the obstetric population.

The fluids to be used in resuscitation have been the subject of a long-lasting debate. As a function of the higher cost of colloids and their side effects such as increased odds of bleeding and kidney disease, as shown in a recent study and a Cochrane review published in 2012,[41,42] crystalloids are preferred for severely ill patients as whole, and albumin infusion should be considered for cases that remain hypovolemic following infusion of large crystalloid amounts.[37] Pregnancy does not represent a contraindication for vasopressors and/or inotropic agents. However, dopamine and noradrenaline might reduce the uteroplacental blood flow while they improve the maternal state. Therefore, when those drugs are used, greater attention must be directed to fetal vitality.[43,44] The latest recommendations by Surviving Sepsis Campaign[37] indicate noradrenaline as the first choice, while adrenaline or vasopressin might be added in special situations or when the patient remains hypotensive despite the administration of large noradrenaline doses. Dopamine should only be used in very specific situations because it is associated with more severe side effects.[45]

Dobutamine infusion should be considered for cases of sepsis associated with myocardial dysfunction and/or continuous signs of tissue hypoperfusion despite fluid resuscitation and normal blood pressure. No data on the use of dobutamine in pregnant women could be found,[46] and the risk that dobutamine might pose to fetal vitality should be assessed.

Importantly, samples for laboratory tests, including complete blood count, blood biochemistry, liver and kidney function, coagulation profile, arterial blood gases, blood glucose and microbiological cultures, should be collected as early as possible, as they serve as therapeutic guides and predictors of prognosis.

As mentioned above, individuals with septic conditions tend to progress into acidemia, which is mainly the result of increased anaerobic metabolism with consequent lactate production. Therefore, monitoring of the arterial lactate levels during treatment represents an important tool to assess response to treatment and improve the accuracy of the prognosis predictions.[47-50]

The aim of initial hemodynamic resuscitation is to restore tissue perfusion to an adequate level and to ensure that cell metabolism and oxygen supply return to normal levels to avoid acidemia and consequent MODS.[51] For pregnant women, one further aim of initial hemodynamic resuscitation is to improve fetal vitality.

Airway maintenance and adequate oxygenation

As a result of the increased systemic vascular permeability that also affects the lungs, sepsis might be accompanied by non-cardiac pulmonary edema and consequent hypoxemia. In such cases, oxygen should be promptly administered by nasal cannula, nebulizers or eventually invasive mechanical ventilation (IMV).

Acute lung injury (ALI) and adult respiratory distress syndrome (ARDS) are frequent occurrences. Most affected patients require IMV, which should be applied as a strategy for lung protection and therefore with low tidal volume (6mL/kg of ideal weight) and low plateau pressure (<30mmHg). The studies that have assessed less-damaging IMV modalities did not include pregnant women.[52-54]

A further point deserving attention concerns the use of sedative and/or neuromuscular blocking agents during IMV, as those drugs are able to cross the placenta and cause a reduction in fetal heart rate variability and fetal movements, thus hindering proper monitoring of fetal vitality.[32]

It is important to address that the targeted oxygen peripheral saturation must be 95% in pregnant women, thus differing from other populations, in which it can be set at 90%. The reason for this difference is the high propensity for and the devastating effects of fetal hypoxemia.

Control of the source of infection and early antibiotic treatment

Blood cultures must be immediately collected upon suspicion of sepsis in addition to urine and airway and surgical wound secretion cultures following their clinical presentation within the first hour of management. Empirically selected antibiotics must be initiated immediately after culture collection and should not be delayed in case unforeseen circumstances prevent the performance of the diagnostic tests mentioned above.

Early onset and appropriate choice of antibiotics exert a direct influence on the survival odds. The antibiotic selection should be based on criteria such as the following: the patient's personal history, infection site, and institutional microbial prevalence.[55] Infections caused by group A beta-hemolytic streptococcus and *Escherichia coli* have been reported to represent the most prevalent causes of lethal sepsis in the peripartum period.[56]

The use of multiple antibiotics is usually avoided in the overall population to prevent the development of bacterial resistance. However, many infections in pregnant women have a polymicrobial origin; broad-spectrum antibiotic therapy is preferred in this situation, such as the combination of penicillin, an aminoglycoside, and clindamycin, vancomycin, or piperacillin-tazobactam.[11,13,57]

Unfortunately, the pharmacological properties of several antibiotics are altered in pregnant women, including a greater distribution volume and modifications in their absorption and excretion, eventually reducing the serum drug levels, particularly in the case of antibiotics excreted in the urine. In addition, some antibiotics are unsafe for the fetus.[58,59]

In parallel, the source of infection must be actively investigated, aiming at its removal. Surgical treatment has paramount importance in cases of abscesses or other pus collections, including the exploration of an infected abdominal cavity, pus drainage, debridement of necrotic tissue, or debridement and drainage of surgery-related pus collections.

Birth must be induced in cases with chorioamnionitis,[11] following a thorough analysis of its risks and benefits jointly performed by the obstetric and ICU staff.

Glycemic control

The indication of strict glycemic control in septic patients is a subject of controversy in the literature. One study conducted in 2001 found that strict glycemic control was associated with a significant reduction in mortality[60] and morbidity in clinical patients admitted to ICU.[61]

However, those results were not reproduced in other studies including NICE-SUGAR,[62] in which the mortality of the group subjected to stricter glycemic control (27.5%) was higher than the group subjected to a more liberal regimen (24.9%).

Therefore, it is recommended to maintain blood glucose levels at approximately 150mg/dL and to avoid hypoglycemic events as far as possible. In addition, the blood glucose level should never be >215mg/dL or, preferentially, >180 mg/dL.[63]

When glycemic control involves continuous intravenous insulin infusion, the capillary blood glucose should be monitored on an hourly basis.

Additional measures

Use of corticoids

The indication of corticoids and blood transfusion in septic patients is subject of controversy in the literature.

A study published in 2002[64] found significant mortality and morbidity reduction when corticoids were administered to patients with septic shock. Those results point to a possible deficiency in the adrenal response in such cases.

However, the more recent CORTICUS study[65] failed to find mortality reduction upon comparing treatment with corticoids in low dose versus placebo in septic patients. In addition, the group subjected to corticoid treatment exhibited higher rates of super-infection, resulting in novel episodes of sepsis or septic shock. Once more, pregnancy was a criterion of exclusion inall of those studies.

The Surviving Sepsis Campaign[37] suggests that hydrocortisone should be administered exclusively to cases of sepsis with refractory shock, i.e., patients who remain hypotensive following initial fluid resuscitation or those who require increasing doses of vasoactive drugs. In such cases, hydrocortisone should be administered at a dose of 200 mg/day by continuous infusion, while a bolus should be avoided due to the risk of hyperglycemic peaks.

Corticoids are usually indicated within the first seven days of treatment and should be interrupted as soon as the patient exhibits signs of clinical improvement and no longer requires vasopressors. In addition, the use of corticoids in high doses or even any kind of corticotherapy is contraindicated in cases of sepsis without shock, unless it is required for other reasons.

One particular confounding factor in the case of pregnant women is the need for corticoid infusion to accelerate fetal lung maturation due to the risk of premature birth.[66]

Blood transfusion

Hébert et al.[67] did not find beneficial differences upon comparing a more liberal regimen of packed red blood cell transfusion versus a stricter transfusion strategy. That study was criticized with regard to the criteria for patient inclusion, as the study included individuals staying in the ICU for more than three days, i.e., beyond the critical phase of disease. In addition, in this study, pregnancy was an exclusion criterion.

The classical study by Rivers[39] found mortality reduction when the hematocrit (Ht) was maintained >30% by means of packed red blood cell transfusion. However, as management included various other measures, the results associated with the Ht level are biased.

As a rule, transfusion is indicated when the hemoglobin concentration[65] is <7.0g/dL, aiming to maintains levels between 7.0 and 9.0g/dL, with concomitant assessment of the patient's comorbidities.[37]

A less strict transfusion strategy is accepted for pregnant women. Transfusion is indicated when fetal vitality is altered despite appropriate fluid resuscitation. In addition, when birth must be induced, significant blood loss is potentially expected, which might further impair fetal perfusion as well as delivery itself, as it increases oxygen consumption.[32]

Prophylaxis

Avoidance of deep vein thrombosis

Because of the state of hypercoagulability induced by both pregnancy[68] and sepsis,[24,69] prevention of deep vein thrombosis is of paramount importance. Prophylaxis includes the use of compression stockings, intermittent lower limb compression, and low molecular weight or unfractionated heparin[37] in addition to stimulation of early ambulation.

When the induction of birth is indicated, pharmacological prophylaxis should be preferentially discontinued for 12 hours prior to avoid significant bleeding.

Avoidance of stress ulcers

Gastric or duodenal ulcers related with the severe clinical status induced by sepsis are known as stress ulcers and occur during the stage of shock.[70] Therefore, the use

of H2 receptor antagonists (H2RAs) or proton-pump inhibitors (PIPs) is indicated in such cases.[37]

Gastroesophageal reflux increases during pregnancy. Under such circumstances, H2RA use is preferred based on the available evidence for drug safety in pregnant women. However, PIPs are not contraindicated if they are required in more severe cases.[71]

Avoidance of hospital-acquired infection

Protocols that include minimal sedation, bed head elevation >45º, oral cavity hygiene, and early IMV weaning are associated with a reduced occurrence of ventilator-associated pneumonia.[72]

Infections associated with urinary catheters are the main source of hospital-acquired infections. For that reason, protocols that restrict the use of urinary catheters and indicate their placement under aseptic conditions and early removal contribute to reduce hospital-acquired infections originating in the urinary tract.[73]

Prophylactic measures to prevent central line-associated bloodstream infections include the following: hand washing, application of barrier and asepsis precautions before and after catheter manipulation, avoidance of catheter insertion in the femoral vein, avoidance of the use of central lines for sample collection, early catheter removal, and daily checking of the puncture site.[74]

Avoidance of excessive and prolonged use of broad-spectrum antibiotics is one additional essential measure to prevent the occurrence of hospital-acquired infection by multidrug-resistant bacteria.

Enteral early nutrition

Feeding must be instituted as soon as possible and preferentially per enteral route to avoid the risk of bloodstream infection associated with parenteral nutrition using a central line and prevent bacterial translocation and thus improve the patient's immunity.[75]

Fetal treatment

As previously mentioned, the best approach to ensure fetal vitality is to stabilize the mother's condition. Although fetal vitality must be judiciously assessed along the full progression of maternal sepsis, no study has yet analyzed the best approach for fetal vitality assessment under this circumstance.

As the main fetal consequences of maternal sepsis primarily derive from vascular changes and poor fetal perfusion, Dopplerfluxometry, umbilical artery Doppler assessment in particular, may represent the best approach to assess fetal wellbeing.

Absent or reversed diastolic flow occurs more often in cases with poor placental perfusion, pre-eclampsia, and fetal growth restriction, and its persistence is associated with an increased rate of neonatal complications and a higher risk of fetal death.[76,77]

Cardiotocography is the test most widely used to assess fetal vitality; however, it has not proven effective in reducing fetal mortality in high-risk pregnancies, as in the case of pregnant women with sepsis.[78]

FINAL CONSIDERATIONS

The incidence of sepsis is steadily increasing in the overall population as well as among pregnant women. Sepsis is one of the main causes of admission of pregnant women to the intensive care units and of maternal mortality.

Despite the latest advances in the treatment of sepsis, its morbidity, mortality, and treatment costs remain substantial.

While pregnancy induces particular physiological changes, there are no evidenced-based recommendations for the treatment of sepsis in pregnant women.

Therefore, the intensive care units staff and obstetricians should work together to improve the management of sepsis during pregnancy.

RESUMO

Sepse é definida por síndrome da resposta inflamatória aguda secundária a um foco infeccioso. Associa-se a elevadas taxas de incidência, morbidade e mortalidade, gerando importante gastos financeiros, especialmente por causas de suas complicações, como choque séptico e disfunção de múltiplos órgãos. As toxinas dos patógenos, associadas à suscetibilidade individual, culminam com a liberação de citocinas capazes de promover resposta inflamatória aguda sistêmica, sendo esta uma das responsáveis pela disfunção de múltiplos órgãos e eventual óbito do paciente.

Especificamente em relação a gestantes, as taxas de incidência e morbimortalidade são menores, dado que as mesmas representam um grupo mais jovem e com menos

comorbidades. A etiologia mais comum nesse grupo é de origem polimicrobiana.

A gestante apresenta particularidades fisiológicas que conferem características específicas na apresentação clínica e laboratorial da sepse nesse grupo. Assim, o melhor conhecimento dessas alterações é fundamental para melhor identificação e condução dessas pacientes. A presença do feto também confere singularidade na abordagem das mesmas.

O tratamento da sepse baseia-se em algumas diretrizes que foram construídas após importantes ensaios clínicos, os quais, infelizmente, sempre tiveram as grávidas como fator de exclusão.

Assim, extrapola-se o tratamento da sepse para a população em geral também para a população de gestantes, sendo as principais metas: manutenção da perfusão tecidual com reposição volêmica e drogas vasoativas (ressuscitação inicial); oxigenação adequada; controle do foco infeccioso e antibioticoterapia precoce; controle glicêmico; infusão de corticoide e transfusão sanguínea quando bem indicadas; profilaxias e, especificamente, vigilância e manutenção da vitalidade fetal.

Descritores: Sepse; Gravidez; Complicações infecciosas na gravidez

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