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# Uroseptic Complications in Pregnant Women with Urinary Tract Infection

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**Abstract** Maternal sepsis is a life-threatening condition, accounting for approximately 15% of obstetric mortality. Urosepsis is a pathological process in which the clinical manifestations of urinary tract infection are complicated by the development of systemic dysfunction. The etiology of urosepsis is determined by its site of onset and the patient's medical history, including particular attention to the use of antibacterial medications, hospitalization in the previous 3 months, and invasive procedures. Pregnancy is an underlying risk factor contributing to the development of systemic inflammation, as it contributes to impaired urodynamics. Impaired urine flow is the primary cause of the transition from a localized inflammatory process to a systemic one. Therefore, urosepsis is considered a pathological process in which the clinical manifestations of a urinary tract infection are complicated by the development of organ systemic dysfunction. Furthermore, changes in immunological reactivity during pregnancy make a woman's body susceptible to infections in general.

**Keywords** Urosepsis, Pregnancy, Urinary tract infections, Pyelonephritis

## 1. Introduction

Urosepsis is a life-threatening organ dysfunction caused by dysregulation of the response to urinary tract infection. Urosepsis occupies a special place among the various types of sepsis due to both its characteristics and high frequency. The proportion of urosepsis is 31.4% of all clinical forms of sepsis, with two-thirds of patients being women. In 25% of cases, urosepsis is a complication of acute pyelonephritis. If an infection is established as the causative factor, then the subsequent development of complications of the disease in the form of bacterial shock and sepsis can be assumed [1,4]. In most cases of urosepsis, pathogens are representatives of the Enterobacteriaceae family, and Escherichia coli ranks first. At the same time, multiresistant pathogens can be detected after urological interventions - Klebsiella pneumonia, Pseudomonas spp. Proteus spp., Serratia spp., Enterobacter spp. [5]. Several risk factors for obstetric sepsis have been identified, leading to the widespread implementation of recommendations for sepsis prevention in this vulnerable group of patients. Currently, screening and treatment for asymptomatic bacteriuria (present in 27% of pregnant women) and sexually transmitted diseases are implemented in early pregnancy, as well as antibiotic prophylaxis during labor and the postpartum period [6].

Increased plasma volume during pregnancy and progesterone -induced vasodilation allow women to maintain compensation for longer during rapid deterioration. Furthermore, elevated white blood cell counts are common during pregnancy, making this indicator less useful in predicting an activated host immune response [7]. Signs of systemic inflammation can be observed at various stages of labor and the postpartum period as a result of the use of prostaglandins for induction of labor or treatment of postpartum hemorrhage. Therefore, a thorough history, detailed clinical examination, symptoms, and clinical examination data are essential for the early diagnosis of obstetric sepsis in this vulnerable group of patients [8].

Hyperthermia is often the first sign that increases physician suspicion for obstetric sepsis; however, body temperature alone is not a reliable indicator. In the Michigan Maternal Death Series, 73% of women who died from sepsis had a normal body temperature, and 25% were afebrile during their hospitalization. Particularly worrisome signs include tachypnea, neutropenia, hypothermia, and altered consciousness.

The decision to prolong the pregnancy depends on several factors, including the patient's condition, gestational age, and fetal well-being. Attempts at early delivery in patients with severe cardiovascular compromise due to sepsis may increase the risk of both maternal and fetal mortality. If the risk of adverse outcome with prolongation of pregnancy outweighs the risk of early delivery, antenatal hormone therapy and magnesium sulfate should be considered to improve fetal outcomes in the event of preterm labor. The decision to deliver is primarily the responsibility of the obstetrician-gynecologist, although the opinion of the anesthesiologist-intensivist may be important in assessing the mother's condition. Treatment of urosepsis is based on

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the general principles of sepsis treatment and includes elimination of the cause (urinary tract obstruction, foci of infection), adequate measures to support vital functions and adequate antibacterial therapy [9]. One of the goals of sepsis treatment in the perinatal period is to maintain oxygenation and perfusion of vital organs and the placenta, as well as identifying the source of infection and targeted treatment. In the antenatal period, intensive care of the pregnant woman is key to ensuring the well-being of the fetus. Infusion therapy is one of the initial measures to maintain hemodynamics and, above all, cardiac output. The main goals of infusion therapy in patients with sepsis are: restoration of adequate tissue blood flow, normalization of cellular metabolism, correction of homeostasis disorders, reduction in the concentration of septic cascade mediators and toxic metabolites. The genitourinary tract is colonized by a wide variety of microorganisms. Not all of them cause infection and sepsis, but pregnant women who develop sepsis are likely to be infected with more than one microorganism.

Therefore, a broad-spectrum antibiotic should be the initial agent of choice, and its selection should be based on local recommendations and resistance patterns, particularly if the source is unknown. Since group A Streptococcus (GAS) and E. coli are the most common causes of sepsis during pregnancy and a significant proportion of deaths, empirical coverage should include these organisms. Initial empirical therapy should include broad-spectrum antibiotics or combinations of several antibiotics that cover the spectrum of possible pathogens in the initial regimen. Subsequent antibacterial therapy should be adjusted based on the results of bacteriological testing. Empirical antibacterial therapy should not be continued for more than 3-5 days; subsequent treatment should be guided by the susceptibility of microorganisms to drugs. The effectiveness of antibacterial therapy is assessed daily in individual patients. The average duration of antibacterial therapy is 7-10 days, but it can be extended [10]. Compared with vaginal delivery, cesarean section results in a 5-20-fold increase in the risk of infection and morbidity: this risk can be significantly reduced with preoperative antibiotic prophylaxis. Collaboration between a team of interested, related specialists is essential not only for the management of patients with urological sepsis but also for the paradigm of modern medicine. To illustrate the complexity of treatment and management of obstetric patients with urological sepsis, we provide our own clinical observation as an example. This patient experienced an exacerbation of right-sided pyelonephritis with a septic course. In modern obstetrics, sepsis remains a significant cause of maternal and perinatal morbidity and mortality. However, current research predominantly focuses on a generalized approach to sepsis in pregnant women, ignoring the diversity of infection sources and etiologic factors.

Obstetric sepsis remains a leading cause of maternal and perinatal morbidity and mortality [1,2]. Despite this, most researchers approach sepsis in pregnant women from a general perspective, without identifying individual etiologic factors and sources of infection. Insufficient attention is paid to the analysis of specific locations of the primary infectious focus, particularly urinary tract infections (UTIs). A similar trend is observed with regard to sepsis risk factors, which are often considered without regard to the location of the primary process [3,4].

Gestational urosepsis is a severe infectious and inflammatory complication resulting from infection of the urinary tract and accompanied by a systemic inflammatory response, an increased risk of multiple organ failure, and death for both mother and fetus [5].

It should be noted that the International Classification of Diseases, 10th revision, does not include the term "urosepsis" as a distinct nosological entity. In clinical practice, cases of gestational urosepsis are most often coded as acute pyelonephritis in pregnancy (O23.0–O23.9), pregnancy-associated sepsis (O85), or other urinary tract infections (N39.0). This complicates the classification and diagnosis of this condition, especially in obstetric hospitals, where sepsis of a urological origin may be regarded as a purulent-inflammatory complication without a precise indication of the source. Risk factors for the development of gestational urosepsis include a history of chronic UTIs (pyelonephritis, cystitis), abnormalities in the development of the urinary system, urolithiasis, anemia, excess body weight - body mass index (BMI) > 25 kg/m2 - etc. However, their role in the development of gestational urosepsis has not been fully studied [6].

Pyelonephritis is a common extragenital disorder during pregnancy, occurring in 8-12% of pregnant women. Its exacerbation during gestation is facilitated by a combination of hormonal, fluid-electrolyte, immune, and mechanical factors inextricably linked to pregnancy. Beginning in early pregnancy, 80% of healthy women experience functional changes in the urinary tract, manifested by decreased tone and hypokinesia of the ureters. This leads to the development of vesicoureteral reflux, increased intra-pelvic pressure, and renal pelvic reflux, leading to the penetration of urine, microbes, and toxins into the kidney tissue, predisposing to the development of acute pyelonephritis or exacerbation of chronic pyelonephritis. Complicated pregnancy with this kidney pathology occurs in 82.3-89%. Currently, there are numerous recommendations for the treatment of this pathology, including empirical antimicrobial chemotherapy for pyelonephritis during pregnancy. However, it should be kept in mind that even the most potent drug therapy, including antibacterial therapy, may be ineffective if urinary obstruction persists. Therefore, the decisive factor in the treatment of obstructive forms of the disease is the restoration of adequate urodynamics using various methods of renal pelvis drainage.

Urinary tract infections are a group of diseases frequently encountered in clinical practice, and this primarily affects pregnant women, who develop functional changes in the urinary tract from early pregnancy. The most common pathological condition during pregnancy is asymptomatic bacteriuria. Late administration of antibacterial drugs, without regard to the sensitivity of pathogens, or insufficient

therapeutic doses can lead to ascending infection, leading to gestational pyelonephritis and other pregnancy complications. Antibacterial therapy is recommended for treatment. To prevent recurrence, cranberry extract containing proanthocyanidin A or other proven herbal remedies are recommended. Regular follow-up is essential for this group of patients.

Thus, identifying and systematizing risk factors for gestational urosepsis in pregnant women with urinary tract diseases is crucial for developing effective preventive measures, timely diagnosis, and early initiation of therapy, which ultimately contributes to the reduction of maternal and perinatal mortality.

## 2. Materials and Methods

Urinary tract infections (UTIs) are a common pathological condition (primarily affecting pregnant women), frequently diagnosed by obstetricians and gynecologists. Physiological pregnancy is characterized by varying degrees of functional changes in the UTIs, including impaired tone and contractility of the muscles of the minor calyces, renal pelvis, and ureters, as well as their dilation. These changes occur early in pregnancy (6-8 weeks), peaking at 18-20 weeks, and contribute to an increased risk of developing UTIs. While hormonal factors are the primary cause of dilation of the renal pelvis and ureters in early pregnancy, mechanical factors also become involved, potentially leading to pyelectasis and vesicoureteral reflux, creating conditions conducive to the development of an ascending infectious and inflammatory process [1-3].

The most common pathological condition during pregnancy is asymptomatic bacteriuria, which occurs in 2–8% of women (with the peak incidence occurring between 9–17 weeks) and is typically detected during a routine examination [4]. A urinary tract infection is indicated by the detection of more than 6–8 leukocytes per high-power field in the midstream urine. Pathogens: Escherichia coli is the primary pathogen causing urinary tract infections, accounting for 60–90%. Additionally, Klebsiella, Enterococcus, Staphylococcus aureus, and other microorganisms may be detected in the urine of patients [5,6].

**Diagnosis.** To diagnose asymptomatic bacteriuria, in addition to a general urinalysis, two consecutive urine cultures using a catheter are recommended. The presence of the disease is indicated by the detection of more than 105 CFU per 1 ml of urine. Identification of the microorganisms and determination of the microbial flora's susceptibility to antibiotics and antibacterial agents are essential. In clinical practice, treatment is most often initiated upon a single detection of 105 CFU/ml or more in 1 ml of urine [7], especially if the urine is neutral.

**Therapy.** Treatment includes a course of antimicrobial, anti-inflammatory, herbal, and physical therapy. Of the antibacterial drugs, penicillins (amoxicillin/clavulanate at a dose of 500 mg 2 times a day for 3-7 days) and cephalosporins (cefixime 400 mg 1 time per day for 5-7 days, ceftriaxone 1000 mg 1 time per day for 3-5 days) can be used. It should be remembered that the use of nitrofuran drugs in pregnant women is limited due to the risk of developing anemia in the mother and fetus [8]. Fosfomycin is considered safe for use during pregnancy [9] and is as effective as ampicillin/clavulanate, but is easier to use (3000 mg once in the treatment of asymptomatic bacteriuria and cystitis) [10]. However, given that fosfomycin cannot deeply penetrate the urothelium, its use is limited and is indicated only in the initial stages of the process and with the early initiation of treatment. Antibacterial therapy for asymptomatic bacteriuria leads to a significant reduction in the incidence of gestational pyelonephritis [11].

If therapy is not carried out, or antibacterial drugs are prescribed without taking into account the sensitivity of the pathogen, or are used in insufficient therapeutic doses, an ascending infection may develop in 30-40% of pregnant women, leading to the development of gestational pyelonephritis. Moreover, about 53% of cases of acute pyelonephritis occur in the second trimester, 26% - in the third [12]. The course of acute pyelonephritis is characterized by an increase in temperature to 38 ℃, dysuria, pain in the lumbar region, weakness. Treatment of acute gestational pyelonephritis should be carried out in a hospital setting. In case of intoxication caused by the inflammatory process, detoxifying, desensitizing, and antispasmodic therapy is indicated. Antibacterial therapy should be prescribed taking into account the sensitivity of microorganisms to antibiotics. Intravenous administration of antimicrobials is more effective. For treatment, a combination of ampicillin + gentamicin, as well as cefazolin + ceftriaxone, can be prescribed, which have approximately equivalent efficacy against microorganisms that cause pyelonephritis [13]. As in the treatment of asymptomatic bacteriuria, for the treatment of pyelonephritis, the use of β-lactams is currently preferred, since the resistance of E. coli to these drugs, according to data, is the lowest [14]. At the same time, an opposite conclusion was made: resistance of E. coli and other microorganisms to ampicillin is 90%, amoxicillin/clavulanate (Augmentin) - 78%, ceftriaxone - 35% [15].

## 3. Discussion

The obtained data indicate the presence of significant associations between the development of gestational urosepsis and a number of clinical and anamnestic characteristics, including a history of urinary tract diseases and infections, congenital urinary tract anomalies, and concomitant gynecological pathologies. The absence of between-group differences in key indicators (age, pre-pregnancy BMI) indicates comparability of the groups and allows us to exclude the influence of these factors on the interpreted differences.

Our results confirm the important role of previous urinary tract pathology in the development of adverse infectious and inflammatory complications of pregnancy. It was established that urolithiasis increases the risk of gestational urosepsis by

4.2 times, and chronic pyelonephritis by almost nine times. These data are consistent with the results of recent studies, according to which the presence of structural or inflammatory changes in the urinary tract in pregnant women significantly increases the likelihood of ascending infection and septic complications [7]. Particular attention should be paid to congenital anomalies of the urinary tract, which, as shown in our study, are associated with the highest risk of infection and the development of uroseptic complications. Thus, congenital anomalies of the urinary system, such as incomplete duplication of the kidney and horseshoe kidney, increase the risk of gestational urosepsis. Thus, pre-pregnancy screening of women with urinary tract anomalies is extremely important, as indicated in a number of modern studies [7,8]. It has been previously reported that duplication of the ureter and renal pelvis can lead to urinary stasis and the development of chronic infection, especially during pregnancy due to physiological changes in urodynamics [7,9]. Differences in the incidence of bacterial vaginosis, chronic salpingitis, and oophoritis in pregnant women with acute pyelonephritis support the hypothesis of the potential influence of the vaginal microbiota and chronic inflammatory processes in the female genital organs on the development of ascending urogenital infection. This is consistent with modern data on the role of the vaginal microbiome and its dysbiotic changes in the development of infectious and inflammatory diseases of the genitourinary system [10].

It should also be emphasized that there were no statistically significant differences between the groups in the incidence of circulatory diseases, anemia, and gastrointestinal diseases, which once again confirms the relevance of the findings and excludes the possibility that such conditions influence the risk of urosepsis in the studied cohorts.

In this regard, in the context of increasing resistance of uropathogens to most antibacterial drugs, the role of third-generation cephalosporins in the treatment of uncomplicated urinary tract infections is increasing. Distinctive features of this group of antibiotics include high activity against microorganisms of the Enterobacteriaceae family, resistance to β-lactamases, and a long half-life, which allows these drugs to be prescribed 1-2 times per day [7]. American scientists conducted a comparative multicenter study of the efficacy of third-generation cephalosporin cefixime and amoxicillin in 565 adult patients suffering from uncomplicated urinary tract infections. The clinical efficacy of cefixime was 90%, while that of amoxicillin was 83%. Uropathogen eradication was observed in 92% of patients treated with cefixime and 84% of patients taking amoxicillin [8]. However, studies have identified multidrug-resistant microorganisms in 95% of urine samples collected from pregnant women with urinary tract infections [9]. Increasing microbial resistance has been noted in the results of many studies [10]. As more and more antibiotics become ineffective, new approaches to treating infectious processes are needed. During exacerbations between courses of antibacterial therapy, as well as to prevent exacerbations of chronic inflammatory processes in the urinary tract, the use of herbal diuretics, antiseptics, and anti-inflammatory drugs should be recommended. Phytotherapy The active components of medicinal plants used to treat urinary tract and kidney diseases (centaury, lovage, rosemary, madder, stolon dicarp, ligulate saxifrage, bearberry, sage, rose hips, St. John's wort, horsetail, etc.) promote the elimination of harmful substances from the body and have antibacterial, anti-inflammatory, anti-allergic, and diuretic effects. Cranberry has also been used for a long time to treat kidney and bladder diseases [12]. The berries of this plant contain organic acids (including salicylate), fructose, vitamins C, A, K, E, and B vitamins, flavonoids, anthocyanidins, catechins, and triterpenoids. Anthocyanidins and proanthocyanidins, which are part of the plant, are natural antibiotics [11]. Their mechanism of action is to inhibit the adhesion of bacteria, including E. coli, to urothelial cells, which facilitates the removal of microorganisms from the urinary tract.

The anti-adhesive effect of proanthocyanidins is dose-dependent and reliable, as confirmed by numerous experimental and clinical studies [4]. Furthermore, the substances contained in cranberry juice alter the composition of urine, preventing the growth of pathogenic bacteria. To achieve an antibacterial effect, drinking natural cranberry juice 2-3 times daily is recommended. However, this treatment can cause adverse effects, the most common of which are belching, nausea, heartburn, increased bowel movements, headaches, increased blood glucose levels, and skin reactions. Therefore, the use of cranberry extract in capsules rather than whole fruits has recently been considered more promising.

## 4. Conclusions

Given the high incidence of urinary tract infections during pregnancy, prevention of this pathology is extremely important. Some clinicians believe it is appropriate to prescribe prophylactic courses of antibacterial therapy (1-3 days), while others dispute the appropriateness of this approach, considering the risk-benefit ratio of this therapy for the mother and fetus. Moreover, frequent, short-term administration of antibacterial drugs contributes to the development of microbial resistance, allergies, immune system impairment, dysbiosis, etc. Therefore, the widespread use of herbal remedies is recommended to prevent exacerbations of chronic pyelonephritis and cystitis. Practical recommendations: Thus, the use of modern herbal remedies, including those based on cranberry products, plays a significant role in the complex of preventive measures aimed at preventing recurrent urinary tract infections. Maintaining personal hygiene, a healthy regimen, a diet excluding spicy and salty foods, and engaging in therapeutic exercise are also mandatory. Every woman should be under the strict supervision of an obstetrician-gynecologist throughout her pregnancy, especially during the critical periods (22-28 weeks), when pyelonephritis in pregnant women most often manifests. Patients with kidney disease require regular follow-up with a general practitioner at a prenatal clinic, including regular screening. This facilitates the early detection of asymptomatic

bacteriuria, the prevention of complications, and the timely initiation of treatment. The findings highlight the need for a comprehensive diagnostic approach to identifying and treating somatic and urogenital diseases in pregnant women. Identifying high-risk pregnant women will enable timely implementation of preventive measures aimed at preventing severe infectious complications, including urosepsis.

Women who have had infectious or inflammatory urinary tract infections (including proteinuria, hematuria, pyuria, increased blood pressure, or edema) during pregnancy, as well as those who have experienced late toxicosis during previous pregnancies, should undergo careful examination and monitoring during all subsequent pregnancies, with mandatory therapeutic and preventive measures. Wider dissemination and implementation of complementary and alternative therapies into routine clinical practice is an effective method for reducing the incidence of inflammatory urinary tract infections during pregnancy.

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