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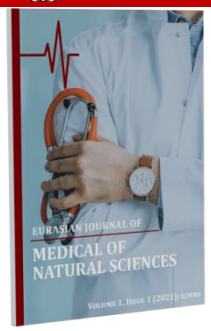

GESTATIONAL PYELONEPHRITIS: COMPLICATIONS, IMMUNE ALTERATIONS, AND MATERNAL-FETAL OUTCOMES

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ABSTRACT

Fifty pregnant women aged 18 to 36 years diagnosed with gestational pyelonephritis were enrolled in the study. Of these, 20 patients presented with acute primary pyelonephritis in either the serous or purulent inflammatory stages, while 30 were diagnosed with chronic pyelonephritis, either in remission or experiencing disease exacerbation. In cases of acute pyelonephritis, urinary tract obstruction and impaired urine drainage were common complications, which required a range of medical interventions. Specifically, ureteral catheterization was carried out in 21 cases, ureteral stents were placed in 6 patients, percutaneous nephrostomy was performed in 3, one patient underwent nephrostomy with infection source decontamination, and another required nephrectomy. Renal function parameters and indicators of endogenous toxicity were evaluated. A strong association was found between elevated levels of middle molecular weight substances (MMS) in both maternal and fetal bloodstreams, especially pronounced in purulent compared to serous forms of the infection. Autoantibodies (auto-Abs) targeting renal antigens were measured in maternal blood serum as well as in umbilical cord blood samples from the newborns. Women affected by pyelonephritis tended to exhibit lower levels of natural physiological auto-Abs, which normally contribute to fetal protection—this finding points to a potential state of mild immunosuppression during infection.

ГЕСТАЦИОННЫЙ ПИЕЛОНЕФРИТ: ОСЛОЖНЕНИЯ, ИММУННЫЕ НАРУШЕНИЯ, МАТЕРИНСКИЕ И ПЛОДОВЫЕ ПОСЛЕДСТВИЯ

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ABSTRACT

В исследование были включены 50 беременных женщин в возрасте от 18 до 36 лет с диагнозом гестационный пиелонефрит. Из них у 20 пациенток выявлен острый первичный пиелонефрит в стадии серозного или гнойного воспаления, тогда как у 30 диагностирован хронический пиелонефрит в фазе ремиссии или обострения. У пациенток с острым пиелонефритом часто наблюдались осложнения в виде обструкции мочевыводящих путей и нарушения оттока мочи, что потребовало различных лечебных вмешательств: катетеризация мочеточников была проведена у 21 пациенток, установка уретерального стента — у 6, чрескожная пункционная нефростомия — у 3, нефростомия с санацией очага инфекции — у 1, а у одной пациентки выполнена нефрэктомия. Оценивались параметры функционального состояния почек и показатели эндогенной интоксикации. Выявлена выраженная зависимость между повышением уровня молекул средней массы (МСМ) в крови матери и плода, особенно при гнойных формах пиелонефрита по сравнению с серозными. Уровни аутоантител (ауто-АТ), направленных против почечных антигенов, определялись в сыворотке крови беременных женщин и в пуповинной крови новорождённых. У пациенток с пиелонефритом отмечалась тенденция к снижению концентрации физиологических естественных ауто-АТ, выполняющих защитную функцию по отношению к плоду, что может свидетельствовать о наличии умеренной иммуносупрессии на фоне инфекции.

Relevance. According to the literature, pyelonephritis ranks as the second most common human disease after respiratory tract infections, with a statistically significant predominance of cases occurring in women [2]. Pyelonephritis is an infectious-inflammatory condition affecting the renal interstitium, tubular apparatus, and the walls of the calyceal and pelvic systems of the kidney, and is caused by various microbial pathogens [2].

In women, the most common causative agents are conditionally pathogenic microorganisms from the intestinal group—*Escherichia coli*, *Klebsiella*, *Proteus*, among others. Notably, polymicrobial associations are identified in 25–30% of cases. The incidence of acute pyelonephritis during pregnancy increased in the 1980s and 1990s, reaching 18–20% [3].

Pregnancy predisposes to both the onset and exacerbation of acute renal inflammation. Contributing factors include impaired urodynamics of the upper urinary tract and vesicoureteral-pelvicalyceal reflux. Additional pathophysiological mechanisms include renal parenchymal hypoxia due to disrupted circulation, which is influenced by common neural regulation of the upper urinary tract, and mechanical compression of the urinary tract by the gravid uterus in conjunction with hypotonia and dilation of these structures [4].

The pathogenesis of acute pyelonephritis in pregnancy involves a multifactorial etiology. Critical factors include the anatomical and functional characteristics of the female urinary system, urinary flow disturbances in the upper tract, asymptomatic bacteriuria in pregnant women, and asymptomatic bacteriospermia in their male partners [1].

Two clinical forms of pyelonephritis are distinguished: acute and chronic. Acute pyelonephritis may manifest as a serous or purulent condition, with the latter possibly progressing to necrotizing papillitis. The purulent form may present as apostematous pyelonephritis, renal carbuncle, or renal abscess. Chronic pyelonephritis typically alternates between periods of remission and exacerbation.

Gestational pyelonephritis refers to pyelonephritis occurring in pregnant women, parturients, and women in the postpartum period.

The aim of this study is to examine the specific features of pregnancy and labor management in women diagnosed with pyelonephritis, to characterize the course of delivery, to assess renal function and indicators of endogenous intoxication, as well as to evaluate the levels of natural autoantibodies in affected mothers.

Materials and methods. This study encompassed 50 pregnant women aged between 18 and 36 years diagnosed with gestational pyelonephritis. Among them, 20 patients presented with acute primary pyelonephritis in either the serous or purulent inflammatory stages, while 30 were diagnosed with chronic pyelonephritis, either in remission or experiencing disease exacerbation. Notably, 5 of these patients had a solitary functioning kidney. The duration of chronic pyelonephritis among participants ranged from 2 to 20 years. Eight patients exhibited concurrent urolithiasis, two had hydronephrotic transformation, and four presented with renal developmental anomalies. One patient had undergone ureteroplasty twice—once at 3 months and again at 3 years of age. Another patient, suffering from chronic pyelonephritis and urolithiasis, underwent ureteral transplantation at 1 month of age due to congenital bladder exstrophy.

Among the five patients with a solitary kidney, one developed acute purulent pyelonephritis during her first pregnancy, necessitating a right-sided nephrectomy and left-sided nephrostomy. This pregnancy was complicated by intrauterine fetal demise at 27 weeks gestation.

In cases of acute pyelonephritis, urinary tract obstruction and impaired urine drainage were common complications, which required a range of medical interventions: ureteral catheterization was performed in 21 patients, ureteral stents were placed in 6, percutaneous nephrostomy was conducted in 3, one patient underwent nephrostomy with infection source decontamination, and another required nephrectomy. The onset of acute pyelonephritis or

exacerbation of chronic pyelonephritis occurred between 10 and 38 weeks of gestation, with 41% of cases arising between 24 and 28 weeks.

Among the study cohort, 25 were primigravida and primiparous. Fourteen patients had a history of induced abortions, including three due to missed abortions, and 12 had experienced spontaneous abortions. Six patients had a history of preterm or term deliveries, with 16 having undergone operative deliveries. Gynecological conditions were identified in 23 patients, including salpingo-oophoritis, cervical erosion, and metroendometritis following abortions and deliveries. Sexually transmitted infections were detected in 10 patients, encompassing chlamydia, mycoplasmosis, ureaplasmosis, and genital herpes.

During the current pregnancy, 26 patients developed gestosis of varying severity, including five cases of preeclampsia and eclampsia. Threatened miscarriage during the first and second trimesters was observed in 19 women, and 23 experienced a risk of preterm labor.

Thirty-six pregnant individuals exhibited reduced kidney function, as indicated by glomerular filtration rates fluctuating between 57 and 85 mL/min/1.73 m^2 (a normal value exceeds 90 mL/min/1.73 m^2). Among eight patients with a history of preeclampsia and eclampsia, the average creatinine level was 57.9 ± 2.1 μmol/L, contrasting with the typical level above 90 μmol/L.

Analysis of urine samples using the Nechiporenko method showed an increased concentration of leukocytes, reaching 6200 ± 120 cells per milliliter. Analysis of two dozen pregnant individuals experiencing severe combined gestational disorders revealed a statistically significant elevation ($p < 0.01$) in circulating medium-sized molecule (MSM) levels. Spectrophotometric analysis at 254 nm yielded an average MSM concentration of 0.44 ± 0.03 arbitrary units (AU), while at 280 nm, the average was 0.46 ± 0.06 AU. This indicates a notable surge in bloodborne MSM in pregnant women with both pyelonephritis and complicated gestational hypertension compared to typical values ($p < 0.05$).

Existing scholarly work generally reports a lack of substantial differences in MSM concentrations between maternal and neonatal blood samples. These variations appear to be contingent upon the intensity of the gestational disorder, the degree of kidney dysfunction, and the functional status of the placental unit [11]. Our findings largely align with these published observations. However, a unique case involved a pregnant patient with chronic pyelonephritis whose pregnancy was further complicated by a flare-up of genital herpes. In this instance, umbilical cord blood exhibited markedly higher MSM concentrations than the mother's blood (0.35 AU at 254 nm and 0.39 AU at 280 nm versus 0.32 AU and 0.31 AU, respectively). The neonate subsequently presented with indicators of intrauterine infection.

Urinary MSM concentrations in pregnant women diagnosed with pyelonephritis were significantly elevated compared to normal ranges (0.44 ± 0.06 AU at 254 nm and 0.46 ± 0.04 AU at 280 nm, against typical values of 0.31 AU and 0.44 AU at the same wavelengths, $p < 0.05$).

The observed increase in MSM concentration served as a predictive marker for renal inflammatory processes, a finding corroborated by sonographic imaging. Assessment of MSM levels in amniotic fluid (predominantly fetal urine) revealed a notable increase in only one

instance, corresponding to a newborn exhibiting signs of intrauterine infection. Strikingly elevated MSM levels in both blood and urine were evident in pregnant women suffering from acute suppurative pyelonephritis (reaching 0.64 ± 0.08 AU at 254 nm and 0.67 ± 0.04 AU at 280 nm). Similarly, umbilical cord blood from newborns in this subgroup displayed increased MSM concentrations (up to 0.65 ± 0.01 AU at 254 nm and 0.66 ± 0.04 AU at 280 nm).m. Our observations indicate that the initial presentation or worsening of pyelonephritis during pregnancy typically occurs between the 24th and 38th gestational weeks. Upon hospital admission, these expectant mothers commonly exhibit systemic signs of toxicity, including elevated body temperatures of 38°C or higher, alongside reports of fatigue, diaphoresis, and headaches. Notably, localized symptoms are often subtle, posing a diagnostic challenge for pyelonephritis. The interdisciplinary nature of this condition is highlighted by the hospitalization of these patients across various specialties: three were transferred from infectious disease units, two from internal medicine wards, and four from surgical departments to our care.

Diagnostic confirmation relies on both the clinical presentation and supplementary evidence obtained through renal ultrasonography, as well as laboratory analyses of blood and urine samples.

Our therapeutic approach for acute pyelonephritis in pregnancy, informed by a collaboratively designed protocol and contemporary insights into the disease's origins and progression, encompasses several key strategies:

1. Re-establishing unimpeded urinary flow from the affected kidney and ureter.
2. Administration of targeted antibacterial agents.
3. Implementation of intravenous fluid and detoxification measures.
4. Interventions focused on sustaining the pregnancy and optimizing the intrauterine milieu for fetal well-being, including mitigating threatened abortion symptoms and preventing fetal oxygen deprivation.

The restoration of urinary drainage from the compromised renal unit and ureter is achieved through internal stenting using either a standard ureteral catheter or a pigtail Stent catheter, guided by real-time ultrasound. Our findings suggest that the pigtail Stent offers certain benefits over the traditional ureteral catheter [5]. Alternative methods include percutaneous nephrostomy and open surgical nephrostomy combined with the removal of purulent inflammatory collections.

The selection of an appropriate upper urinary tract drainage technique for pregnant individuals with acute pyelonephritis necessitates careful consideration of several factors: the duration of the acute episode, the specific microorganisms involved, the extent of dilation within the renal collecting system, and the current stage of pregnancy [7].

The initial choice of antibacterial agents involved ampicillin and oxacillin, leveraging the broad-spectrum activity of semi-synthetic penicillins and cephalosporins against prevalent gram-positive and gram-negative bacteria. Their comparatively minimal fetal impact makes them particularly suitable during the critical first trimester, coinciding with organogenesis.

However, the effectiveness of these semi-synthetic penicillins was limited in nearly one-third of cases (31.6%) due to the widespread resistance of *E. coli* strains and the inherent

insensitivity of *Klebsiella spp.* [12]. In such instances, combination penicillins like amoxiclav and augmentin were favored for their enhanced antimicrobial action against the primary urinary tract infection agents encountered during pregnancy. Notably, these drugs achieve therapeutic concentrations not only in urine but also within the kidney tissue itself, crucial for effectively managing pyelonephritis in expectant mothers [12].

Beyond the first trimester, treatment regimens expanded to include cephalosporins, nitrofurans (such as nitroksolin), nalidixic acid derivatives, and later-generation (third and fourth) cephalosporins, alongside the continued use of semi-synthetic penicillins. Aminoglycosides, specifically gentamicin, were reserved for the postpartum period.

For severe, treatment-refractory urinary tract infections, the carbapenem class of antibiotics (including imipenem, tienam, and meropenem) proved efficacious [12]. It is crucial to note the recommendation to discontinue nalidixic acid and pipemidic acid before delivery, as existing literature suggests a potential link to increased intracranial pressure in the fetus. Furthermore, these agents are contraindicated in patients with significant kidney or liver impairment.

Antibiotic dosages were carefully adjusted based on individual glomerular filtration rates. The duration of antibiotic therapy typically spanned 10 to 14 days. Complementary treatment included herbal remedies such as phytolysin (for its anti-inflammatory properties), chophytol (to support nitrogen excretion and liver function), and canephron (a multi-component herbal formulation with diuretic, antispasmodic, vasodilatory, anti-inflammatory, and antibacterial effects) [13].

A cornerstone of the comprehensive management of acute pyelonephritis was intravenous fluid therapy. Commonly administered solutions included crystalloids like Ringer's-Locke solution, isotonic saline, 4% sodium bicarbonate, and 5–10% glucose. In select cases, albumin administration (100 ml of 10–20% amino acid solutions, e.g., Alvезин), providing essential amino acids, was deemed necessary.

In conclusion, evaluating markers of internal toxic buildup and the immunological profile of pregnant individuals with pyelonephritis is crucial for initiating prompt and comprehensive treatment, thereby mitigating the detrimental effects of infection on the developing fetus. Elevated levels of endogenous toxins and alterations in immune parameters serve as indicators of potential intrauterine infection, necessitating supplementary therapeutic interventions for pregnant women with pyelonephritis. Given the elevated infectious burden observed in our patient cohort, meticulous attention should be directed towards the duration of broad-spectrum antibiotic administration during the postoperative phase. The combination of early diagnostic measures and appropriate therapeutic strategies effectively prevented the recurrence of pyelonephritis in the postpartum period. Employing assessments of kidney function and markers of internal intoxication enabled the identification of subclinical inflammatory processes in a subset of patients, allowing for the timely implementation of targeted antibacterial treatment. Both in the immediate aftermath and the long term following gestational pyelonephritis, consistent outpatient monitoring by a urologist is essential, alongside thorough examinations of infants born to mothers who experienced this condition.

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