Case Report

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# The Significance of *E.Coli* Treatment in Perinatal Period

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## SUMMARY

**Introduction:** Bacteriuria of pregnancy is a common condition.
**Case report:** Patient, 30-years, pregnant woman. During pregnancy, *E. coli* infection recurred in 4 times, applied Cephalexin and Ceftriaxone. The delivery was terminated by CS, GW 38; girl infant, AS 9. After the period of lactation: secretory status - the patient was a secretor of A and H blood type substance; ultrasonography and contrast radiography - presence of the third kidney. The therapy was added by vaccine UroVaxom, and there was no *E. coli* infection during 2 years follow up period. The Child is now 7 years old girl, having brilliant psychomotorical development. Possible child brain damage, lung damage, mental diseases are the reason for necessity *E. coli* infection treatment during pregnancy.
**Conclusion:** All pregnant women should be screened for bacteriuria. *E. coli* is most commonly sensitive to group B antibiotics (cephalexin and amoxicillin), safe to be included in pregnancy. Long-term follow up of infants born from mothers having bacterial infection during pregnancy is necessary.

**Keywords:** pregnancy, *E.coli*, infection, pregnancy, sequelle, cephalosporins, cephalexin, penicillins, amoxicillinh

## NOTE

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## INTRODUCTION

Bacteriuria of pregnancy is a common condition which is thought to be associated with serious sequelae in mother and fetus. Most women acquire bacteriuria before pregnancy, while 20%-40% of women with asymptomatic bacteriuria will develop pyelonephritis during pregnancy [1].

Treatment of asymptomatic bacteriuria lowers this risk. Most symptomatic urinary tract infections (UTI) in pregnant women present as acute cystitis. Short-term therapy is not as established as in non-pregnant women. In the last 10 years, the drugs of choice for *E. coli* UTI treatment have been amoxicillin and cephalexin. Resistance rate in *E. coli* is generally about 40%. During pregnancy, quinolones and tetracyclines are contraindicated in the first trimester, while sulphonamides should not be used in the last trimester [2,3].

Lower socioeconomic standard due to population migration in the countries in transition increases the frequency of these infections in women in generative period [4].

The objective of this paper was the reevaluation of the knowledge on the significance of the urinary tract *E. coli* infections during perinatal period through the summary of the contemporary reviews from the aspect of gynecologists, hospital clinical pharmacologists, transfusiology specialists, microbiologists, urologist, nephrologists and radiologist using one clinical case report as illustration.

## CASE REPORT

A patient, 30-year old, was referred to clinical pharmacologist for correction of the antibiotic treatment of the recurring *E. coli* urinary infection. During two years, she was treated by parenteral antibiotics of different groups according to drug susceptible test but no eradication of the urinary infection was achieved. The patient's expectations were directed towards the selection of "the exclusive drug". During conversation, the patient was sleepy and complained of that she failed to become pregnant as wanted in the last 2 years. A clinical pharmacologist first requested differential diagnostics to rule out the pregnancy. Laboratory analyses and ultrasonography confirmed the pregnancy of 6 gestation weeks and it implied the choice of antibiotics most appropriate for pregnancy. The patient is a blood type A secretor meaning that she is not predisposed to *E. coli* infection.

Cephalexin (group B) (Palitrex®, Galenika, Serbia) caps. 500mg in dose 3 x 1, a oral form of I generation cephalosporin, was included in her therapy, as the only sensitive antibiotic according to drug susceptibility test, meaning that there are no reported side-effects in pregnancy. During pregnancy, *E. coli* infection recurred in months 4 and 6, and each time the cephalexin was applied on the basis of drug susceptibility test. In the 8th month, the infection recurred the third time with more manifested picture. Upon laboratory tests and ultrasonography, the decision was made to manage the infection by i.m. Ceftriaxone (group C) (Longaceph®, Galenika, Serbia), a parenteral form of III generation cephalosporin, in dose of 2 x 1 gr. The patient developed hypertension, 150/90 mmHg and mild edemas of the extremities. She underwent amniocentesis in gestation week 38, L/S=1.5:1, what indicated inadequate lung maturation; with a view to accomplish the lung maturity, the fetus was administered with i.m. dexamethasone (Dexasone®, Galenika, Serbia), in a dose of 4 g, and intraamniotic Ceftriaxone (Longaceph®, Galenika, Serbia) of 1 g. Upon artificially accomplished lung maturity, L/S>3:1in gestation week 38. The delivery was terminated surgically by a Cesarian section in the gestation week 38. It was a live-born, healthy infant with crown-to-toe=48cm, BW=3200 g, head circumference=35cm, and Apgar score=9. The postoperative course was uneventful and the wound healed per primam (by first intention).

After delivery, the patient developed recurring infections what urged doctors to examine her urinary tract thoroughly.

Laboratory diagnostics and drug susceptibility test were repeated. After the 10 months period of lactation, secretory status was determined and contrast urography was carried out. Secretory status was determined by inhibition of hemagglutination in thermally processed saliva, on what occasion it was found that the patient was a secretor of A and H blood type substance (Technical Manuel AABB).

The ultrasonography and contrast radiography revealed that both kidneys secreted adequately and evenly. Two ureters were viewed to the right, and both had extended lumen suggesting the presence of the third kidney. The ureters joined at the level of SI joint,

worked as one and just before their confl uence to the urinary bladder they were constricted. The urinary bladder had usual confi guration. Medical Board decided that there was no indication for surgical intervention. The therapy was added by vaccine. Upon the prescribed vaccine preventive treatment (UroVaxom®, OM Pharma, Switzerland), 1 capsule daily on an empty stomach, for 3 consecutive months the patient has been infection-free over two-year period of follow up. The Child is now 7 years old nice girl, having brilliant psychomotorical development. The doctors' team is proud with the results and prevention of possible serious consequences of *E.coli* infection from pregnant female patient to her newborn.

## DISCUSSION

To date, the UTI in pregnant patients has been explained by obstruction of the urine outfl ow in gravid uterus. This relatively simple interpretation does not consider the receptor etiology of the ascending UTI and/or gestational adaptation of the immune system [5].

Gestational pyelonephritis is associated with multiple complications, such as fetal growth retardation, preterm labour, cerebral palsy, septicemia and maternal death, and is characterized by microbial invasion of the renal interstitial tissue. In case of congenital anatomic abnormalities of the urinary tract, the risk of complications becomes higher [6].

Both the biological complexity and molecular epidemiology of the UTI suggest that obstruction/stasis is not the only factor leading to the risk of gestational UTI. The data seem to be inconsistent with the interpretation that obstruction/urine stasis is the main cause of UTI in pregnant women[7].

Pregnancy modulates immunity through diverse and still incompletely defi ned mechanisms. Placental proteins suppressed both the cellular and humoral aspects of the immunity. Both hormones, progesterone and glucocorticoids, share important anti-infl ammatory and immunosuppressive properties, having potent anti-proliferative effects in MLR, mitogen activation and cytotoxic T-cell generation. Immunosuppression is supported by placental protein 14 and by local inhibition of the TNF-α pathway [5,8].

*E.coli* has B-like antigen, so the individuals with B and AB blood types are susceptible to this urinary infection. Moreover, it is well known that non-secretors of blood type substances are more susceptible to infections than secretors [9, 10, 11]. Women non-secretors of B and AB blood types are particularly susceptible to recurring urinary tract infections. Enzymatic synthesis of blood group B-like antigen revealed that the biosynthetic pathway of B antigen was essentially the same in *E. coli* strains as in humans. The uroepithelial cells of non-secretors tended to greater adherence of the uropathogenic *E. coli* when compared to secretors. Radiolabeled E. coli had higher affi nity of binding to extended globo-series, Sialosyl formed from glycosphingolipids extracted from the nonsecretors [12]. Our patient has A blood type, and she is a secretor of A and H substance; accordingly, by this criterion, she does not belong to any risk group [10, 13].

According to some authors, asymptomatic infections, bacteriuria, do not call for treatment. However, the experimental studies on rabbits (animal model which resembles most the humans by chronological development of the alveoli) showed that untreated infection led to decreased respiratory alveolar surface (by 25%), leukomalacia, and postnatal retarded growth (by 60%) [14, 15].

The newborns weighing less than 1500 g born from mothers who had received parenteral antibiotics during their pregnancy were at lower risk of cystic periventricular leukomalacia than the infants from the same category whose mothers had not been given antibiotics during their pregnancy [16, 17]. Many meta-analysis indicates that chorioamnionitis is a risk factor of cerebral palsy [4, 18, 19].

Mother's reaction to the infection, the production of cytokines and antibodies, compromises the integrity of the fetal-pla¬cental link. Researchers report fi ndings of the elevated cytokines in the plasma of pregnant women whose offsprings later develop schizophrenia [20, 21]. Maternal or placental infection increases the risk of moderate to severe NE (neonatal encephalopathy), not just sepsis. The clinical evaluation of NE should include consideration of the maternal infection, examination of the placenta, and use of the neonatal markers of infection/infl ammation [5, 22, 23, 24].

Early maternal antibiotic therapy delays white matter cell death in rabbit fetuses exposed to intrauterine infection.

This may provide a window for pre-

venting the white matter damage [14, 25, 26].

Screening for asymptomatic bacteriuria and treatment is recommended for selected groups such as pregnant women, where benefi t has been shown [2, 3].

The safety data of many other antibacterials in pregnancy, including carbapenems, ketolides and streptogramins, are very limited or lacking. Extensive clinical experience shows that penicillin, cephalosporin and erythromycin (except erythromycin estolate) can be considered safe both for developing fetus and pregnant woman [2, 27]. Therefore, all pregnant women should be screened for bacteriuria and subsequently treated with antibiotics [1, 28, 29]. Nevertheless, modern clinical pharmacology considers the individual therapeutical approach to patient the most important [30].

## CONCLUSION

Preclinical studies unquestionably point to irreversible changes of fetal brain in case of mother's untreated urinary infection. In human population, long-term follow up of pregnant women and their infants is necessary for such decision-making.

All pregnant women should be screened for bacteriuria and subsequently treated with antibiotics. Since *E. coli* is most commonly sensitive to group B antibiotics (cephalexin and amoxicillin), it is safe to include them in cases of symptomatic and asymptomatic bacteriuria during pregnancy.

The implementation of prospective observational clinical studies phase IV may improve the outcome of pregnancy, prevent and allow for early diagnostics and treatment of the urinary infections of a mother, what will make the establishment of good guidelines easier.

Nevertheless, modern clinical pharmacology considers the individual therapeutical approach to patient the most important and the most promissing.

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# Značaj tretmana *E.coli* tokom trudnoće

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## KRATAK SADRŽAJ

**Uvod:** Bakteriurija je česta u trudnoći.
**Prikaz slučaja:** Pacijentkinja, 30 godina, trudnica. Tokom trudnoće imala je infekciju *E.coli* 4 puta, kada je lečena Cefaleksinom i Cefriaksonom. Porodila se carskim rezom, u 38 NG, rodila je zdravo žensko dete, Apgar skor 9. Nakon perioda laktacije: Sekretorni status pokazuje da je pocijentkinja sekretor A i H *blood type substance*. Ultrazvučni pregled i radiografija sa kontrastom pokazuje prisustvo trećeg bubrega. U terapiju je uključena vakcina *UroVaxom*, nakon koje nije bilo recidiva infekcije E.coli tokom 2 -godišnjeg perioda praćenja. Dete je sada 7-godišnja zdrava devojčica sa odličnim psihomotornim razvojem. Moguća ozbiljna oštećenja mozga, oštećenja pluća i psihička oboljenja koja mogu nastati kod deteta kao sekvele nelečene infekcije *E.coli* tokom trudnoće majke, su razlog za obavezno lečenje infekcije *E.Coli* tokom trudnoće.
**Zaključak:** Neophodan je skrining svih trudnica na bakteriuriju. Kako je *E.coli* najčešće senzitivna na grupu B antibiotika (Cefaleksin i Amoksiciklin) bezbedno je uključiti ih kod asimptomatske i simptomatske bakteriurije u trudnoći. Neophodno je višegodišnje praćenje dece čije su majke u trudnoći imale bakterijske infekcije.

**Ključne reči:** trudnoća, *E.coli*, infekcija, sekvele, cefalosporini, cefaleksin, penicilini, amoksiciklin

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