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Evaluation of Infections in Hospitalised Pregnant Women

Hastaneye Yatırılarak Tedavi Edilen Gebelerde Saptanan Enfeksiyonların Değerlendirilmesi

Burcu ÖZDEMİR[1], Sümeyye KAZANCIOĞLU[1], Esragül AKINCI[1], Cemal Reşat ATALAY[2], Hürrem BODUR[1]

[1]University of Health Sciences, Ankara Numune Health Practice and Research Center, Clinic of Infectious Diseases and Clinical Microbiology, Ankara, Turkey

[2]University of Health Sciences, Ankara Numune Health Practice and Research Center, Clinic of Obstetrics and Gynecology, Ankara, Turkey

Abstract

Introduction: Hormonal and immunological changes in pregnancy may lead to an increase in infectious diseases caused by some pathogens. In this study, we aimed to determine the types of infections and treatment approaches in pregnant women who were hospitalized due to infectious diseases.

Materials and Methods: This retrospective study included 87 pregnant women who were hospitalized in the Infectious Diseases and Clinical Microbiology and Obstetrics and Gynecology Clinics of the University of Health Sciences, Ankara Numune Training and Research Hospital between January 2011 and December 2016.

Results: The median age of the 87 pregnant women was 23 years, and 40 of them were in the second trimester. Analysis of infection diagnoses showed that urinary tract infection (UTI) was the most common infection (59 patients, 67.8%). Most of the patients with UTI developed pyelonephritis (42 patients, 71.1%). Twenty-five patients' urine culture yielded a pathogen in urine culture while *Escherichia coli* was the most common isolate. Seven of the isolated strains were extended-spectrum beta-lactamase (ESBL) producers. Ceftriaxone was started in 35 of the patients with pyelonephritis. Treatment duration was 5-17 days (mean 11 days). Other infections were acute gastroenteritis, pneumonia, influenza, varicella, measles, tularemia, brucellosis, Crimean-Congo hemorrhagic fever, adult-onset Still's disease, acute viral hepatitis A and B coinfection, and perianal abscess.

Conclusion: UTI is the most common infection in pregnant women. *E. coli* is the most commonly isolated microorganism and the rate of ESBL-positive isolates is increasing. Pyelonephritis is more common than other UTI and requires hospitalization.

Keywords: Pregnancy, urinary system infection, brucellosis, CCHF, ESBL

Öz

Giriş: Gebelerde hormonal ve immünolojik değişimler nedeniyle bazı patojenlerin yol açtığı enfeksiyon hastalıklarında artış görülebilmektedir. Bu çalışmada enfeksiyon nedeniyle yatırılarak takip edilen gebelerde saptanan enfeksiyon türleri ile tedavi yaklaşımlarının belirlenmesi amaçlandı.

Gereç ve Yöntem: Çalışmada Sağlık Bilimleri Üniversitesi, Ankara Numune Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği ile Kadın Hastalıkları ve Doğum Kliniği'nde Ocak 2011-Aralık 2016 tarihleri arasında yatırılarak takip ve tedavi edilen 87 gebe hasta retrospektif olarak incelendi.

Bulgular: Çalışmaya alınan 87 gebenin ortanca yaşı 23 olup %46'sının 2. trimesterde olduğu belirlendi. Olguların enfeksiyon tanıları incelendiğinde en sık üriner sistem enfeksiyonlarının (ÜSE) (59 hasta, %67,8) yer aldığı saptandı. ÜSE olan olguların çoğunun (42 hasta, %71,1) piyelonefrit olduğu, piyelonefrit olgularının 25'inin (%59,5) idrar kültüründe üreme olduğu ve üreme olan hastalarda da en sık *Escherichia coli* izole edildiği belirlendi. Etkenlerin yedisinde genişlemiş spektrumlu beta-laktamaz (GSBL) olumlu saptandı. Piyelonefrit tanısı alan hastaların 35'inde seftriakson başlanmıştı. Tedavi süresi 5-17 gün (ortalama 11) idi. Diğer belirlenen enfeksiyonlar akut gastroenterit, pnömoni, influenza, suçiçeği, kızamık, tularemi, bruselloz, Kırım-Kongo kanamalı ateşi, Erişkin Still hastalığı, akut viral hepatit A ve B koenfeksiyonu ve perianal apse idi.

Sonuç: Gebelikte en sık görülen enfeksiyon ÜSE'leridir. Etken çoğunlukla *E. coli* olup GSBL üreten suşların oranı artmaktadır. Piyelonefrit oranı diğer üriner enfeksiyonlardan daha yüksektir ve hastaneye yatırılarak tedavi edilmeyi gerektirmektedir.

Anahtar Kelimeler: Gebelik, üriner sistem enfeksiyonu, bruselloz, KKKA, ESBL

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Address for Correspondence/Yazışma Adresi: Burcu Özdemir MD,
University of Health Sciences, Ankara Numune Health Practice and Research Center, Clinic of Infectious Diseases and Clinical Microbiology, Ankara, Turkey
Phone: +90 541 698 03 85 **E-mail:** burcubagci17@hotmail.com **ORCID:** orcid.org/0000-0002-1851-3539

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Introduction

Although pregnant women are not initially more susceptible to infections, there may be an increase in diseases caused by certain pathogens later in pregnancy due to hormonal and immunological changes. In general, high estradiol concentrations promote $CD4^+$ type 2 T helper cell (Th2) responses and humoral immunity[1]. Progesterone suppresses the maternal immune response and alters the Th1/Th2 balance[2,3].

Urinary tract infections (UTIs) are the most common infections during pregnancy and may affect 20% of women of childbearing age[4,5]. The most important risk associated with asymptomatic bacteriuria (ASB) during pregnancy is the development of pyelonephritis. It is known that pyelonephritis can occur in 20-30% of pregnant women with untreated ASB[6]. Therefore, early diagnosis and treatment of ASB during pregnancy is important.

Pregnant women, children under 2 years of age, adults over 65 years of age, and individuals with chronic illness constitute a high-risk group for seasonal influenza[7]. Pressure exerted by the fetus reduces the expansion capacity of the lungs and limits their ability to expel secretions, resulting in a higher risk of pneumonia for pregnant women[8].

This study was conducted to determine the types of infections detected and the treatment approaches used in pregnant patients admitted to our hospital due to infection. In this way, we aimed to contribute to the epidemiologic data.

Materials and Methods

Eighty-seven pregnant women who were hospitalized and treated on an inpatient basis in the Infectious Diseases and Clinical Microbiology, and the Gynecology and Obstetrics departments of University of Health Sciences, Ankara Numune Training and Research Hospital between January 2011 and December 2016 were retrospectively analyzed. Patient data were obtained from the hospital's electronic medical record system and were recorded in specially prepared forms for each patient. For patients with UTI, midstream urine specimens collected under sterile conditions were plated onto 5% sheep blood agar and eosin-methylene blue agar using quantitative methods. The culture media were evaluated after incubation at 37 °C for 18-24 hours, and culture plates with uniform growth and $\geq 10^5$ CFU/ml were accepted as causative agents. The isolates were identified by conventional methods, and antibiotic susceptibility tests were performed by the Kirby-Bauer disc diffusion method according to the Clinical and Laboratory Standards Institute standards. Extended-spectrum beta-lactamase production was tested by the double disk diffusion method[9]. Influenza was diagnosed by in house real-time polymerase chain reaction (PCR) according to United States Centers for Disease Control and Prevention protocol performed on nasopharyngeal aspirate specimens sent to the Public Health Institution of Turkey. Diagnosis of pyelonephritis was based on the presence of pyuria or bacteriuria in patients with fever (>38 °C), flank pain, or costovertebral angle tenderness, with or without signs and symptoms of cystitis (dysuria, frequent urination, urinary urgency)[9]. Diagnosis of acute gastroenteritis was based on having three or more soft, watery bowel movements per day[10].

Ethical approval was obtained from the Ankara Numune Training and Research Hospital Ethics Committee before initiating the study (date and number of approval: 05.07.2017, 17-1466).

Results

A total of 87 pregnant patients who were hospitalized between January 2011 and December 2016 were included in the study. Their median age was 23 years (range, 17-44 years). Eighty-two of the patients (94.2%) were under 35 years of age. Investigation of the distribution of cases according to stage of pregnancy showed that admissions were most commonly in the second trimester, with 25.3%, 46%, and 28.7% of admissions occurring in the first, second, and third trimesters, respectively. Urinary tract infections were the most common type of infection identified (67.8%), followed by gastroenteritis (Table 1).

The majority of patients with UTI had pyelonephritis (71.1%, n=42). Of the patients diagnosed with pyelonephritis, all had dysuria and 95.2% (n=40) had costovertebral angle tenderness and fever. In addition, 26 patients had hydronephrosis and five patients had nephrolithiasis. Mean white blood cell (WBC) count was 16,290/mm^3. Urine culture yielded a pathogen in 25 (59.5%) of these patients. *Escherichia coli (E. coli)* was most frequently isolated causative agent (Table 2). Seven of the causative agents were extended-spectrum beta-lactamase (ESBL)-positive (2 *Klebsiella pneumonia*, 4 *E. coli*, 1 *Pseudomonas* spp.). Thirty-five of the patients diagnosed with pyelonephritis were started on ceftriaxone, and treatment was changed in 8 of these patients based on their antibiogram results (2 received ertapenem, 4 received meropenem, and 2 received sulbactam/ampicillin). Of the remaining 7 patients, 3 received meropenem, 3 received ertapenem, and 1 received sulbactam/ampicillin. Treatment lasted for 5-17 days (mean 11 days).

Urine cultures yielded a pathogen in 9 of the 15 patients diagnosed with cystitis. *E. coli* was the most common causative agent isolated in culture (n=7) (Table 3). One *E. coli* strain was ESBL-positive. Patients diagnosed with cystitis had a mean WBC count of 12,620/mm^3 and a mean C-reactive protein level of 33.5 mg/L. The patients were treated with ceftriaxone (n=10), ertapenem (n=3), sulbactam-ampicillin (n=1), or cefazolin

(n=1) for a duration of 7-10 days. The patient diagnosed with urosepsis had *E. coli* growth in blood and urine cultures and was treated with ceftriaxone for 14 days.

Evaluation of the relationship between UTI diagnoses and gestational week revealed that most of the patients were admitted during the second trimester (Table 3).

Of the 13 patients with gastroenteritis, five patients with fever and findings of fecal leukocytosis were treated with antibiotics (ceftriaxone for three, metronidazole for two), while the others were provided hydration support only. No pathogenic bacterial growth was observed in fecal cultures. One patient went into labor at 36 weeks of gestation.

Of the patients with respiratory symptoms, four were diagnosed with pneumonia and treated with sulbactam-ampicillin, while three were found to have influenza A and were treated with oseltamivir (five days). Two of the patients with influenza A were in the first trimester and the other was in the second trimester, and none developed complications.

Table 1. Distribution of patients according to infection diagnosis

Diagnosis	Patient number	
	n	%
Urinary tract infections - Pyelonephritis - Cystitis - Urosepsis	59 42 15 2	67.8 48.27 17.24 2.29
Acute gastroenteritis	13	14.94
Pneumonia	4	4.59
Influenza A	3	3.44
Chickenpox	1	1.14
Measles	1	1.14
Tularemia	1	1.14
Brucellosis	1	1.14
Crimean-Congo hemorrhagic fever	1	1.14
Adult-onset Still's disease	1	1.14
Acute viral hepatitis A and B coinfection	1	1.14
Perianal abscess	1	1.14
Total	87	100

Table 2. Causative agents isolated in urine culture

Causative agent	Cystitis	Pyelonephritis
Escherichia coli	7	14
Klebsiella pneumoniae	1	7
Proteus spp.	1	1
Pseudomonas spp.	-	1
Coagulase-negative staphylococcus	-	1
Staphylococcus saprophyticus	-	1
Total	9	25

A woman at 8 weeks of gestation was diagnosed with Crimean-Congo hemorrhagic fever (CCHF) as a result of a tick bite and developed miscarriage following vaginal bleeding and subchorionic hematoma. She was discharged in good condition after 10 days.

A woman at 13 weeks of gestation who was admitted to the obstetrics unit due to thyrotoxicosis, pancytopenia, and elevated liver function test (LFT) results underwent total thyroidectomy and was treated with ceftriaxone and rifampicin for six weeks due to *Brucella* spp. growth in two postoperative blood cultures, and she fully recovered on follow up.

A woman at 29 weeks of gestation was diagnosed with chickenpox and another woman at 24 weeks of gestation was diagnosed with measles. They were both followed with symptomatic treatment and recovered with no complications. A patient at six weeks of gestation with elevated LFT results tested positive for anti-HBc IgM (+) and anti-HAV IgM (+) and was monitored for 6 days with a diagnosis of acute hepatitis A and B coinfection. She was discharged while follow-up LFT results showed regression.

A 22-week pregnant woman with fever and elevated LFT results (alanine aminotransferase: 204 u/l, aspartate aminotransferase: 276 u/l, lactate dehydrogenase: 1675 u/l) was hospitalized with complaints of fever, joint pain, myalgia, and maculopapular rash for ten days. During follow-up, her WBC count decreased to 3600/mm^3 and platelet count decreased to 49,000/mm^3, after which LFT and hemogram values improved. *Brucella* tube agglutination, Rose Bengal, viral hepatitis markers, and TORCH screen (toxoplasmosis, rubella cytomegalovirus, herpes simplex, and HIV) were negative. Parvovirus IgM and PCR were negative, measles IgG was positive, autoimmune (antinuclear antibody, rheumatoid factor, antimitochondrial antibodies) markers were negative, and ferritin level was >2000 ng/ml, and no focus of infection was detected. The patient was diagnosed with adult-onset Still's disease, started on methylprednisolone, and followed in the rheumatology clinic.

Microagglutination assay for tularemia performed on a woman at 27 weeks of gestation with swelling on the left side of her neck and a sore throat yielded a result of 1/320, and the patient was hospitalized with a diagnosis of tularemia. Due to the toxic

Table 3. Number of patients diagnosed with urinary tract infection according to trimester of pregnancy

	First trimester	Second trimester	Third trimester
Acute cystitis	6	3	6
Pyelonephritis	7	24	11
Urosepsis	1		1
Total	14	27	18

fetal effects of the medication recommended to treatment tularemia, the patient refused treatment and was discharged by her own will with recommendation to return for follow-up. However, we learned that the patient did not attend follow-up appointments after discharge.

A perianal abscess was detected in a woman at ten weeks of gestation. She presented with complaints of nausea, vomiting, and perianal pain, and was treated with ertapenem for 14 days.

Discussion

The risk of UTI is higher during pregnancy. Relaxation of the smooth muscles due to increased estrogen and progesterone during pregnancy results in urethral dilation and larger bladder volume, which in turn may lead to urinary stasis and vesicoureteral reflux[11]. This facilitates bacterial migration from the bladder to the kidney and increases the risk of pyelonephritis. Studies have also shown that pyelonephritis occurs most commonly in the second trimester (53%) and is associated with untreated bacteriuria[12-14]. The risk of pyelonephritis can be reduced by treating ASB. Therefore, early diagnosis and treatment of ASB is important during pregnancy. Pregnant women should be screened for ASB and initiated treatment when necessary. Because the data were analyzed retrospectively in this study, it is not known whether the pregnant women diagnosed with pyelonephritis had a history of ASB. In addition, we observed in this study that the majority of pyelonephritis patients were admitted during their second trimester (57.1%). A meta-analysis indicated that the risk of preterm birth and low birth weight was higher in pregnant women with ASB compared to those without[15]. However, there are also studies in which no risk was detected[6,16]. In the present study, we did not detect any pregnancy-related complication in patients with pyelonephritis. No growth was detected in the urine cultures of patients using antibiotics at time of admission, despite the presence of pyuria. In addition, hydronephrosis was detected in the majority of those diagnosed with pyelonephritis in our study, leading to the conclusion that performing urinary ultrasound would be beneficial in patients diagnosed with pyelonephritis.

The causative agents of UTIs in pregnant women and their virulence are similar to those in non-pregnant women[17]. The most common causative agent is *E. coli*. In one study, *E. coli* was identified as the most common causative agent in patients with pyelonephritis, at a rate of 70%[18]. *E. coli* was also found to be the most common causative agent in our study. Increasing antibiotic resistance is an important problem today. Even in uncomplicated UTIs, the prevalence of ESBL-producing strains is increasing[19,20]. In a study conducted in India, it was reported that ESBL-producing uropathogens were a problem for pregnant females[21]. In our study, ESBL positivity was detected in 15.2% (9/59) of patients diagnosed with UTI.

Crimean-Congo hemorrhagic fever is an acute viral infection that can be fatal and has no definitive treatment. Data on CCHF during pregnancy are limited. However, mortality is reported to be higher in pregnant women than in the general population[22]. A review of 41 pregnant women diagnosed with CCHF reported 34% maternal mortality and 58.5% fetal/neonatal mortality[23]. There is no specific antiviral therapy for CCHF and the effectiveness of ribavirin therapy is still being discussed[24]. Our patient had a miscarriage but was discharged in good condition.

Although complications such as miscarriage and intrauterine death are seen in animals due to tularemia, data on infection in human pregnancy are very limited[25]. Tularemia during pregnancy may lead to prematurity or fetal loss. However, healthy newborns who were not adversely affected by maternal tularemia have also been reported[26-30]. There is no consensus regarding the treatment of tularemia during pregnancy. In one publication, two of three pregnant tularemia patients were followed without treatment while one was treated with gentamicin, and it was reported that all three patients reached full term with no maternal or fetal complications[26].

Pregnant women are at a 4-5 times higher risk of influenza A infection compared to healthy non-pregnant women. In addition, the disease course varies between stage of pregnancy, and women at term are hospitalized 5 times more than women earlier in pregnancy or postpartum[31]. Early treatment with antiviral therapy is recommended for pregnant women with suspected influenza. Oseltamivir is a pregnancy category C drug. However, due to the serious complications of influenza, the benefits of antiviral therapy outweigh the potential risks of antiviral drug use in pregnant women[32]. In the present study, all three patients with influenza A were in the first or second trimesters, all received antiviral therapy, and no complications were observed.

Conclusion

In conclusion, the clinical manifestation, disease course, and treatment approach for infections detected in pregnant women vary. This study was conducted to characterize these differences. There are few studies in the literature regarding pregnant women, and more extensive research is needed.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ankara Numune Training and Research Hospital Ethics Committee before initiating the study (date and number of approval: 05.07.2017, 17-1466).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: H.B., C.R.A., E.A., Design: H.B., E.A., B.Ö., Data Collection or Processing: B.Ö., S.K., Analysis or Interpretation: B.Ö., Literature Search: B.Ö., S.K., E.A., Writing: B.Ö.

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