

Research Article

Urinary Tract Infection in Pregnancy: A Study of Pathogen and Bacterial Resistance in Mexico

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Abstract

Background: Urinary tract infection (UTI) is the most common bacterial infection in humans, produced by bacteria known as uropathogenic species. UTI are the most common bacterial infections during pregnancy and there is an association between UTI with preterm labor and low birth weight; Escherichia Coli is the cause of 80% of urinary tract infections in the community. E. coli can become resistant to antibiotics through conjugation, with DNA transfer.

Aim: So the purpose of this study is determine the most frequent pathogen and its antibiotic resistance in pregnant patients with urinary tract infection in Chihuahua, Mexico.

Design and Setting: Descriptive cross-sectional study.

Methods: A total of 395 pregnant patients had urinary tract infection determined by a general urine test or urine culture. Only 101 women had a positive urine culture. The urine samples were collected and processed in the local laboratory. Standard biochemical technique for the identification of microorganisms was used; to determine antimicrobial susceptibility, the Kirby-Bauer method was used and disc reading was performed as recommended by international guides.

Results: A total of 101 patients had a positive urine culture; as etiological agent was found: Escherichia coli 82 (81.2%), Klebsiella 13 (12.8%), Proteus 5 (4.9%), Staphylococcus coagulase negative 1 (0.9%). The most widely used drug was Ampicillin (79%) as well as the one with the highest rate resistance (100%).

Conclusion: Nitrofurantoin and amoxicillin should be the antibiotics of choice in the UTI during pregnancy as described in the Mexican clinical practice guide. The resistance rates to other antibiotics are high.

Keywords: Urinary Tract Infection; Pregnancy; Escherichia Coli

Introduction

Urinary tract infection (UTI) is the most common bacterial infection in humans, produced by bacteria known as uropathogenic species [1]. UTI are the most common bacterial infections during pregnancy. The susceptibility it is increased during gestation due to the hormonal and anatomical changes that contribute to the ectasia of the urine [2]. Pregnant women have an increased risk of urinary tract infections, since at week 6 and week 22-24 approximately 90% of pregnant women develop urethral dilatation [3].

There is an association between asymptomatic bacteriuria with preterm labor and low birth weight. In a recently published meta-analysis, mothers with bacteriuria had a 54% greater risk of having a child with low birth weight and twice the risk of having a preterm birth compared to mothers who did not have bacteriuria [4]. The higher rates of preterm birth are apparently related to the higher prevalence of lower genital tract infections and the increased risk of preterm labor in the context of urinary tract infection. Urinary tract infections are also associated with low socioeconomic status and immunodeficiency [5].

Twenty percent of pregnant women have a urinary tract infection in the course of gestation [6]. The clinical spectrum may range from uncomplicated cystitis to fulminant pyelonephritis due to multiorgan failure. The main microorganisms that cause Urinary Tract Infection are Enterobacteriaceae, especially Escherichia coli and Klebsiella pneumoniae, Escherichia coli is the cause of 80% of urinary tract infections in the community. In pregnant women, the presence of urinary infection increases the risk of spontaneous abortion and preterm birth, which makes this type of infections a public health problem that requires strict vigilance due to its high prevalence [7].

Although the incidence of asymptomatic bacteriuria is similar in pregnant women than in those who are not pregnant, the prevalence of acute pyelonephritis is significantly higher in pregnant women with asymptomatic bacteriuria, 20-30% of untreated asymptomatic bacteriuria during pregnancy will develop acute pyelonephritis, a complication responsible for septic shock in the most severe cases. This is why in the first prenatal control auroculture is routinely performed, whose objective is to reduce the incidence of this serious pathology [8].

The risk factors for UTI are: 1) Organic: vesicoureteral reflux,

Table 1: Frequency of uropathogen in pregnancy.

Uropathogen	N	%
Escherichia Coli	82	81.2
Klebsiella	13	12.8
Proteus	5	4.9
Staphylococcus Coagulasa Negativo	1	0.9

N: Frecuency, %: Percentage.

2) instrumentation: urinary catheterization, endoscopic surgery. 3) Obstructive: Prostate cancer, intrinsic or extrinsic compressive tumors, urethral stenosis and lithiasis. 4) Functional: Pregnancy, bladder dysfunction: neurogenic bladder, incontinence and 5) Structural: malformations (urethral valve, stenosis, ectopic ureter), urinary tract surgery (leads, fistulas, obstructions) [9].

The resistance to antimicrobial agents is generally due to the selection of resistant strains in the environment, or due to the exchange of genetic material among different species. The way that organisms become resistant is the exchange of DNA. Gram-negative species are the most frequently involved in urinary tract infection, such as E. coli, can become resistant through conjugation, with DNA transfer from one member to another [10]. A general urine test is the first step in the laboratory diagnosis of urinary tract infection; however, in a pregnant patient, no studies are necessary to begin treatment with suggestive clinical data. A sample of urine taken under sterile conditions is centrifuged for five minutes and then the pellet is examined at high magnification; the next step in the diagnosis of urinary tract infection is urine culture (gold standard), in this case a count of more than 100,000 CFU/ml (> 10,000 CFU in gram positive or fungi) correlates with infection in most cases [11].

Table 2: Antibigram results (resistance and sensitivity).

	N	Resistance	%	Sensitivity	%
E. Coli	82	Ampicillin	100%	Furazolidone	100
		Tetracycline	100%	Amikacine	100%
		Trimethoprim	99%	Gentamicin	98%
				Nitrofurantoin	97%
				Amoxicillin	62%
Klebsiella	13	Ampicillin	100%	Furazolidone	100%
		Trimethoprim	100%	Amikacine	100%
		Tetracycline	100%	Gentamicin	100%
		Nitrofurantoin	92%	Amoxicillin	31%
Proteus	5	Ampicillin	100%	Amikacine	100%
		Trimethoprim	100%	Gentamicin	100%
		Tetracycline	100%	Amoxicillin	40%
Staphylococcus Coagulasa Negativo	1	Ampicillin	100%	Tetracycline	100%
		Erythromycin	100%	Trimethoprim	100%
		Dicloxacillin	100%	Nitrofurantoin	100%
				Gentamicin	100%

N: Frecuency, %: Percentage.

The most commonly used antibiotics in the treatment of urinary tract infection are: Ampicillin, Amoxicillin, Ampicillin/sulbactam, amoxicillin/clavulanate, cephalothin, cephalixin, cefepime, cefotaxime, ceftriaxone, amikacin, gentamicin, trimethoprim-sulfamethoxazole, azithromycin, ciprofloxacin, levofloxacin, nitrofurantoin, fosfomicin, imipenem, meropenem. For many years, amoxicillin and ampicillin are the antibiotics of choice in the treatment of urinary tract infection, but the high development of resistance by the uropathogenic, especially by E. coli, and the availability of other drugs have reduced their indications. Amoxicillin and ampicillin are useful mainly in pregnant women, in cases where a sensitive bacterium has been isolated. Nitrofurantoin is the treatment of choice during pregnancy and is active against many urinary pathogens, reaches high concentrations in urine but not blood, so it is not useful in bacteremia [11].

The biological mechanisms that precipitate preterm births in women with asymptomatic bacteriuria are unclear; however, gestation has been considered due to the hormonal changes that it causes, it sensitizes the uterus and when pregnancy is complicated by bacteriuria due to gram-negative bacilli, the endotoxin of these microorganisms can theoretically precipitate preterm births [12]. Based on the above, the main objective of this study was to determine the most frequent pathogen and its antibiotic resistance in pregnant patients with urinary tract infection in Chihuahua, Mexico.

Materials and Methods

A descriptive, retrospective and cross-sectional study was carried out in the Gynecology and obstetrics hospital #15 of the Mexican Institute of Social Security (IMSS) in Chihuahua, Mexico, from

January to December, 2014. All the medical records of pregnant women were reviewed and information was collected of Patients that met the following inclusion criteria: age from 18 to 35 years, a history of urinary infection during pregnancy with a positive urine culture. Exclusion criteria were: congenital or pre-pregnancy malformations of the urinary tract, chronic diseases or contaminated sample. To establish the diagnosis of urinary tract infection, a positive urine culture (>100,000 CFU/ml) was required with antibiogram which should be reported in the local laboratory files or in medical records of Patients to determine the most frequent pathogenic agent and their resistance to antibiotics available in our environment, for outpatient and hospital use.

The universe of patients was consisted of 6199 pregnant women during the year 2014; sample was consisted of 395 pregnant patients with a diagnosis of urinary tract infection determined by a general urine test or urine culture, which came for consultation by having urinary symptoms or during routine exams in their prenatal care. Only 101 pregnant women had a positive urine culture. The urine samples were collected with the criteria established to be the first one in the morning, discarding the first portion of the urination and with previous grooming of the genital area to be collected in a sterile bottle; after that the sample was processed in the local laboratory in microbiology area by certified personnel. Standard biochemical technique for the identification of microorganisms was used; to determine antimicrobial susceptibility, the Kirby-Bauer method was used and disc reading was performed as recommended by international guides.

The data obtained was integrated into data collection sheets and analyzed using the SPSS program version 20 in Spanish, where we applied descriptive statistics for qualitative variables use frequencies and percentages. The protocol was authorized by the Local Committee of Research and Ethics in Health Research from the obstetrical and gynecological hospital #15, where the study took place.

Results

The productivity records of the Hospital of Gynecology and Obstetrics #15 of the city of Chihuahua, Mexico, were reviewed, finding 6199 pregnant women during 2014, of which 395 patients had a diagnosis of urinary tract infection, estimating a prevalence of 6.37%; 1983 pregnant women presented some type of complication in the pregnancy (preterm labor or threatened abortion), which corresponds to 32% of the total of pregnant women.

A total of 101 patients had a positive urine culture; as etiological agent was found: *Escherichia coli* 82 (81.2%), *Klebsiella* 13 (12.8%), *Proteus* 5 (4.9%), *Staphylococcus coagulase negative* 1 (0.9%) (Table 1). Regarding our primary objective, the analysis of the sensitivity and resistance of bacteria observed *in vitro*, it was found that *E. coli* is the most frequent bacterium with 83% in the reviewed urine cultures, with a 97% resistance to the treatment used. Followed by *Klebsiella* with 13% and a resistance of 100% to the treatment. *Proteus* was found with 3%, with a 20% resistance to empirical treatment; finally, *Negative Staphylococcus Coagulase* was found with 1%, finding undetermined resistance (Table 2).

The 101 patients with positive cultures were empirically managed with the following antibiotic regimens: Ampicillin 500mg q6h for 7

Table 3: Frequency of empiric antibiotic.

Antibiotic	N	%
Ampicillin	90	90.9
Amoxicillin	4	4.04
Nitrofurantoin	7	7.07
Percent of empirical treatment resistance		100

N: Frecuency, %: Percentage.

Table 4: Frequency of complication in pregnancy with urinary tract infection.

Total pregnancies with confirmed TUI (urine culture)	N= 101
Percentage of pregnant women requiring hospitalization	98%
Reason for hospitalization	
Threatened abortion	34%
Preterm labor	65%

N: Frecuency, %: Percentage.

to 10 days, Amoxicillin 500mg q8h for 7 to 10 days, Nitrofurantoin 100mg q8h for 7 to 10 days. The most widely used drug was Ampicillin 79% of the cases as well as the one with the highest resistance 100% (Table 3). 98% of the patients presented some type of complication during the pregnancy, threatened abortion or preterm labor (Table 4).

Discussion

The most frequent etiological agent of urinary tract infections during pregnancy is *E. coli* with 100% resistance to Ampicillin, being the most used antibiotic in primary care; *E. coli* was associated with a pregnancy complication rate of 98% in patients with positive urine culture. A 100% resistance of the isolated bacteria to the rest of the treatments used in patients with a positive urine culture was also observed. Therefore, based on the data obtained in this study, the treatment used for urinary tract infection in pregnancy should be reevaluated. Replacing ampicillin with amoxicillin or nitrofurantoin would reduce complications in pregnancy (threatened abortion and preterm birth). It was found that even though the patients hospitalized for urinary tract infection had some complication, not all of them had a urine culture.

Conclusion

One of the main theories that explains a greater resistance in pregnancy to beta-lactamics is that there is a bioavailability of only 50% of these drugs, which increases the resistance and agrees with our study in our environment 100% of the isolated *E. coli* were resistant to ampicillin. Although in the Mexican clinical practice guideline for UTI in pregnancy, nitrofurantoin and amoxicillin have a sensitivity of 97 and 92% respectively against *E. coli* in our environment, according to the reviewed urine cultures, a low sensitivity was reported for amoxicillin; however, Nitrofurantoin was in most cases sensitive, so primary care physicians or those who have contact with pregnant patients should adhere to what is described in the Mexican clinical practice guidelines for UTI in pregnancy and start treatment with nitrofurantoin or amoxicillin. The role of ampicillin and other second-line antibiotics as a treatment for urinary tract infection in pregnancy should be questioned because of the results obtained in our study.

References

1. Braun JS, Camponovo CR, Cona TE, Fernández VA, García CP, Heryé EB, et al. Recommendations for microbiological diagnosis of urinary tract infection. *Rev Chil Infect*. 2001; 18: 57-63.
2. Le J, Briggs G, McKeown A, Bustillos G. Urinary System Infections During Pregnancy. *Annals of Pharmacotherapy*. 2004; 38: 1692-1701.
3. Sifontes L. Incidence of urinary infections in the threat of preterm birth in pregnant women. *Ginecología y Obstetricia*. 2011.
4. Estrada-Altamirano A, Figueroa-Damian R, Villagrana-Zesati R. Urinary tract infection in pregnant woman. Importance of scrutiny of asymptomatic bacteriuria during gestation. *Perinatol Reprod Hum*. 2010; 24: 182-186.
5. Noxikova N. Prenatal screening and treatment of lower genital tract infections to prevent preterm delivery. Switzerland: World Health Organization. 2009.
6. Cabrero Roura L. Premature birth. Buenos Aires: Panamericana; 2007.
7. Mendell G, Bennett J, Dolin R. Principles and practices of infectious diseases. 6th ed. Filipinas: Elsevier Churchill Livingstone; 2009.
8. Calderón U, Doren A, Cruz M, Cerda J, Abarzua F. Acute pyelonephritis in pregnancy and antimicrobial susceptibility of uropathogens. *Rev Chil Ginecol Obstet*. 2009; 74.
9. Echeverria-Zarate J, Sarmiento-Aguilar E, Osoreo-Plenge F. Urinary tract infection and antibiotic management. *Acta Med Per*. 2006; 23.
10. Abarzúa F, Zajere C, Donoso B, Belar C, Riveros J, González P, et al. Reevaluation of the Antimicrobial Sensitivity of Urinary Pathogens in Pregnancy. *Rev Chil Ginecol Obstet*. 2012; 67: 226-231.
11. National Center for Health Technology Excellence. Diagnosis and treatment of urinary tract infection in pregnancy. Mexico: Ministry of Health. 2008.
12. Nicolle L, Bradley S, Colgan R, Schaeffer A, Hooton T. Infectious Diseases Society of America Guidelines for the Diagnosis and treatment of Asymptomatic Bacteriuria in adults. *Clinic Infect Dis*. 2005; 40: 643-644.