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ETIOLOGICAL PREVALENCE OF URINARY TRACT INFECTIONS IN SYMPTOMATIC PREGNANT WOMEN IN A HIGH COMPLEXITY HOSPITAL IN MEDELLÍN, COLOMBIA, 2013-2015

Prevalencia etiológica de infección del tracto urinario en gestantes sintomáticas, en un hospital de alta complejidad de Medellín, Colombia, 2013-2015

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ABSTRACT

Objective: To determine the prevalence of urinary tract infections (UTIs) and their microbiological profile and antibiotic resistance in pregnant women with suspected urinary tract infection.

Methodology: Cross-sectional study of pregnant women with suspected community-acquired urinary tract infection referred to the outpatient clinic by prenatal care practitioners or seen in the emergency room, and admitted to a referral teaching hospital located in Medellin, Colombia between August 2013 and September 2015. Pregnant women who had received antibiotics on the day before admission were excluded. Simple random sampling. Measured variables: sociodemographic, clinical and bacteriological. Descriptive statistics were applied.

Results: The prevalence of urinary tract infections was 29%. The predominant isolates were Gram negative bacteria, mainly *E. coli* and *K. pneumoniae* (57.7% and 11.4%, respectively). Resistance to trimethoprim-sulfamethoxazole and to ampicillin-sulbactam was observed in 19.5% and 17.5% of isolates, respectively.

Conclusions: Population-based studies are needed to provide a better approach to bacterial resistance in community-acquired UTIs. On the other hand, the high resistance observed may suggest that some of the exposed antibiotics should not be included in the local guidelines for the management of UTIs.

Key words: urinary infections, infectious complications of pregnancy, urinalysis.

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RESUMEN

Objetivo: determinar la prevalencia de infección del tracto urinario (ITU), el perfil microbiológico y la resistencia a los antibióticos en mujeres gestantes con sospecha de infección del tracto urinario.

Materiales y métodos: estudio de corte transversal. Ingresaron gestantes con sospecha de infección del tracto urinario adquirida en la comunidad, remitidas a consulta externa desde su control prenatal o atención por urgencias, y hospitalizadas entre agosto de 2013 y septiembre de 2015 en un hospital universitario de referencia ubicado en Medellín, Colombia. Se excluyeron gestantes que hubieran recibido antibióticos el día anterior a la admisión. Muestreo aleatorio simple. Variables medidas: sociodemográficas, clínicas y bacteriológicos. Se aplicó estadística descriptiva.

Resultados: la prevalencia de infección del tracto urinario fue del 29 %. Predominaron los aislamientos de bacterias gram negativas, principalmente *E. coli* y *K. pneumoniae* en un 57,7 y 11,4 % respectivamente. Se observó resistencia a trimetoprim-sulfametoxazol en el 19,5 % y ampicilina-sulbactam en el 17,5 % de los aislamientos.

Conclusiones: se requieren estudios de base poblacional para una mejor aproximación a la resistencia de las bacterias causantes de la ITU en la comunidad. Por otra parte, la alta resistencia observada podría sugerir que algunos antibióticos expuestos no sean incluidos en las guías locales de manejo de la ITU.

Palabras clave: infecciones urinarias, complicaciones infecciosas del embarazo, uroanálisis.

INTRODUCTION

Urinary tract infection (UTI) is defined as invasion of the urinary tract by pathogenic microorganisms in a concentration of 100,000 colony forming units (CFUs) or more of the infectious agent, accompanied or not by symptoms. It is classified as complicated or uncomplicated. Uncomplicated infections present as asymptomatic bacteriuria (AB) in the absence of symptoms associated with bacteria grown in urine culture with the CFU count described above, and as cystitis when there are local symptoms such as dysuria, hematuria or pelvic pain in a female with a normal urinary tract. Complicated urinary infections include renal infection (pyelonefritis), which is accompanied by fever and generalized compromise. This category includes infections occurring in patients with functional or anatomical abnormalities of the urinary tract, immunocompromised patients, and pregnant women. UTIs are more frequent in women than in men (1).

In pregnancy, anatomical, hormonal, metabolic and immune changes modify the natural history of UTIs. Asymptomatic bacteriuria is usually benign in non-pregnant women, but the risk of developing pyelonephritis increases during pregnancy (2). Consequently, during pregnancy, screening should be offered for asymptomatic bacteriuria and it should be treated if diagnosed (3), as it should also be done in cases of cystitis and pyelonephritis (4). Another reason for screening and treating UTIs during pregnancy is their association with poor perinatal and maternal outcomes, including preterm delivery, premature rupture of membranes and low birthweight (5). The Cochrane review on asymptomatic bacteriuria in pregnancy, which was published in 2015 and included 14 studies with 2000 women, showed a reduction in pyelonephritis, with a relative risk (RR) of 0.23 (95% CI: 0,13-0,41) and in preterm delivery, with a RR of 0.27 (95% CI: 0.11-0.62) when antibiotic treatment was provided; however, low confidence in the estimated effect of the included studies was found (6). As far as the frequency of UTIs during pregnancy is concerned, the prevalence of asymptomatic bacteriuria in the United States ranges between 5 and 10% (4, 7), while the incidence of cystitis is 1.3% (8) and of pyelonephritis 0.5% (9).

The microorganisms that cause UTIs in pregnant women are the same that have been isolated

in non-pregnant women. In North America, E. coli is the most frequent isolate (70-80%), followed by Klebsiella pneumoniae, Proteus mirabillis, pseudomonas and citrobacter, and Streptococcus hemolyticus among Gram (+) bacteria (10). Sialidase producing microorganisms are isolated less frequently, including S. agalactiae, Prevotella ssp. and Bacteroides ssp. (11). In Latin America, although the distribution is similar, frequency varies. For example, the frequency for E. coli ranges between 25% (12) and 93% (13), and between 7% and 20% for enterococcus (12, 14). Knowledge of local sensitivity of these microorganisms to antibiotics is important because empirical antibiotic treatment is often initiated in cases of symptomatic UTI on the basis of a profile of low local resistance, safety for the fetus and the mother, and good efficacy (4). Information in our setting concerning the etiology of community acquired UTIs during pregnancy must be updated on a permanent basis in order to revise evidenced-based clinical practice guidelines to guide decision-making by clinicians regarding the right antimicrobial agent to use in pregnant women according to prevalent germs and their resistance profile. The purpose of this study was to determine UTI prevalence, etiologic prevalence and resistance to common antibiotics used to treat the causes of this infection in pregnant women seen in a Level III university clinic.

MATERIALS AND METHODS

Design and population. Cross-sectional study of pregnant women referred to the outpatient clinic from prenatal care or the emergency service, admitted on suspected UTI to a referral university hospital in Medellín, Colombia, between August 2013 and September 2015. Pregnant women who had been receiving antibiotics the day before admission were excluded because of the possibility of affecting the urine culture result. A sample of 587 pregnant women was calculated, assuming a base population of 1000 pregnant women with an expected 18% prevalence of UTI confirmed by urine culture, with 95% confidence and a 2% error. Simple random sampling was applied for the selection of the pregnant women.

Procedure. One of the researchers identified the ICD-10 (N30-39, N10, N12, N15, N16) related to the UTI diagnosis during the study period, and it was used to look for the information in the clinical records. Three researchers verified the eligibility criteria and extracted the sociodemographic, clinical and bacteriological data. The diagnosis of urinary infection was confirmed by one positive urine culture on The diagnosis of urinary infection was confirmed by one positive urine culture on Agar Elite CHROMID CPS, which was read by a bacteriologist specialized in microbiology and analyzed by an obstetrician or general practitioner to make the diagnosis and, depending on the number of colonies, is read by a bacteriologist specialized in microbiology and analyzed by an obstetrician or general practitioner to make the diagnosis. All patients received empirical treatment for the infection after taking the urine culture in accordance with the management guidelines of the hospital obstetrics service as adapted from the clinical practice guidelines of the Ministry of Health and Social Protection (Colombia) (15) and the recommendations of the Committee on Infectious Diseases of the Society of Obstetricians and Gynecologists of Canada (16). Antibiotic therapy was discontinued when the result of the culture was negative, continued or modified according to clinical response and results of the sensitivity test. The information was entered in Microsoft Excel 2010 and data validation in the cells was applied in order to avoid typing errors.

The measured variables were maternal age, gestational age at the time of consultation, type of affiliation to the health system, number of pregnancies, history of kidney stones, urinary tract malfor-

mation, gestational diabetes or use of steroids, type of isolate and antibiotic resistance profile, as well as the clinical diagnosis (cystitis, pyelonephritis or asymptomatic bacteriuria).

Statistical analysis. The analysis was performed using the SPSS software package version 20.0. Qualitative variables were summarized with absolute and relative frequencies, and continuous variables were summarized with the median and inter-quartile range (IQR) because they did not follow a normal distribution. The general prevalence of UTIs was described (number of patients with confirmed UTI / total patients admitted). The 95% confidence interval was calculated for UTI prevalence. Etiologic prevalence (number of patients with specific bacteria type / total number of patients with UTI) and bacterial resistance (proportion of specific bacteria resistant to an antibiotic / total isolates of the bacteria) were calculated.

Ethical considerations. This study was considered risk-free and was endorsed by the Health Research Ethics Committee of *Universidad Pontificia Bolivariana of Medellín* and of *Clinica Universitaria Bolivariana*.

RESULTS

A total of 896 clinical records with UTI-related ICD-10 were identified. Of these, 593 entries were selected randomly for review of the clinical records. Overall, 48 were not eligible, and no clinical record was available for 32 patients (5.8%). Of the remaining 513, 99 were excluded because the patients had received antibiotics the day before taking the urine sample for culture. This resulted in 414 patients with clinical suspicion of UTI and with a urine culture; in 291 of them, the urine culture was negative, while the diagnosis was confirmed in 123 pregnant women, for a 29% prevalence of culture-confirmed urinary tract infection in women with clinical suspicion of community-acquired infection (95% CI: 25.4-34.2) (Figure 1). Of these cases, 67 (54%) were classified as cystitis, 44 (36%) as pyelonephritis and 12 (10%) as asymptomatic bacteriuria. First UTI episodes accounted for 52.8% (65).

In terms of baseline characteristics, the median age of the patients was 25 years, most of them were affiliated to the contributive regime of the Colombian social security system, they were all in their first pregnancy and in the third trimester of gestation. Important background history included kidney stone disease (8.9%), urinary tract malformations (4.9%) and gestational diabetes (4.1%) (Table 1).

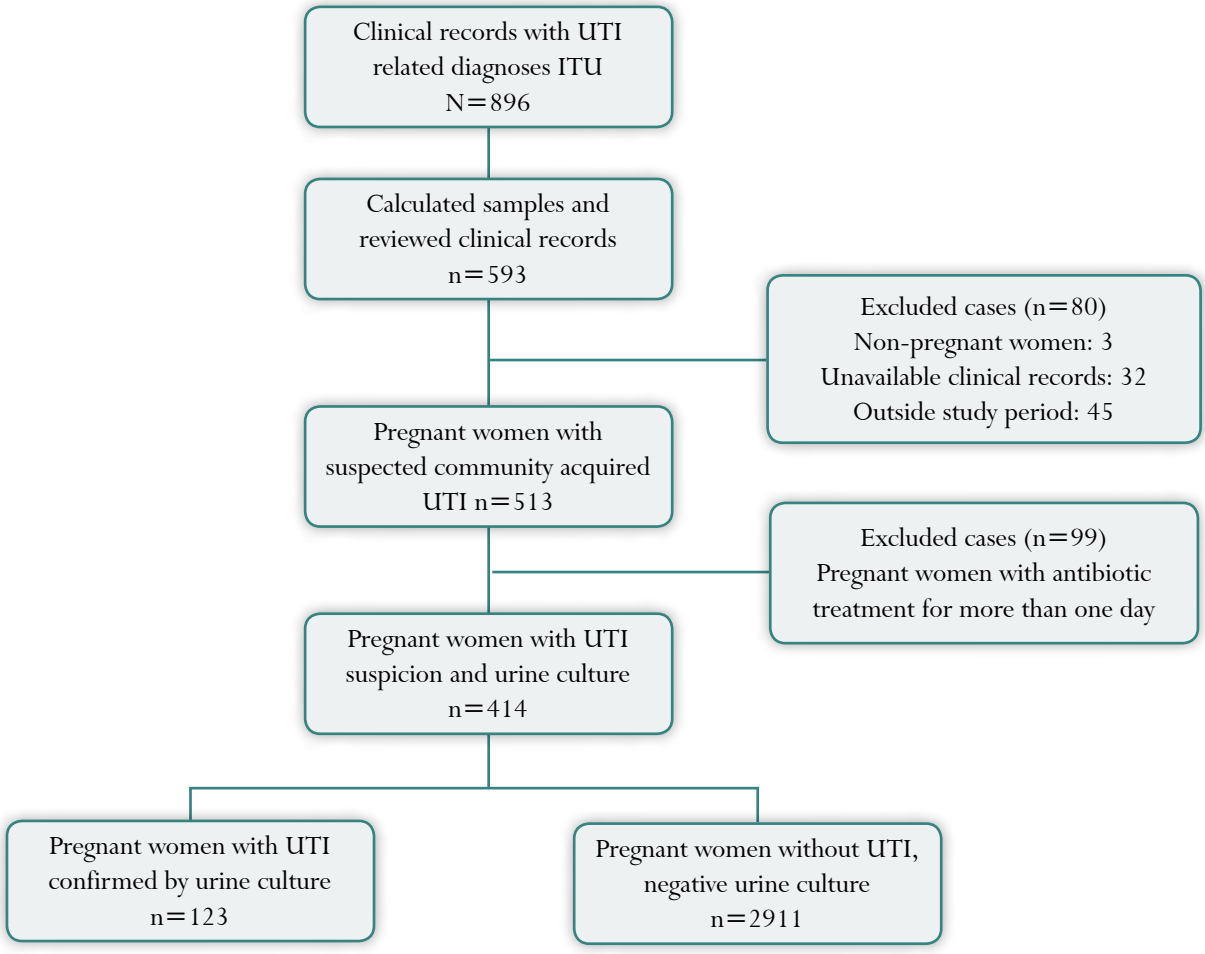
Regarding etiologic prevalence, the most frequent germ was *E. coli,* identified in 71 patients (57.7%), followed by *K. pneumoniae* in 14 (11.4%) and *P. mirabilis* in 9 (7.3%) (Table 2).

Antibiotics with the highest proportion of resistance were trimethoprim-sulphamethoxazole in 24 isolates (19.5%) and ampicillin-sulbactam in 21 (17.5%). Important resistance was found to trimethoprim-sulphamethoxazole (31%), ciprofloxacin (21.1%) and cephalothin (15.5%) in *E. coli;* to ampicillin-sulbactam (21%) and nitrofurantoin (29%) in *K. pneumoniae* and to trimethoprim-sulphamethoxazole (22.2%) and ciprofloxacin (22.2%) in *P. mirabilis*. Resistance to aztreonam was 1.4%. Table 3 shows resistance profiles for the different isolates. In terms of resistance patterns, extended spectrum betalactamases (ESBL) were identified in six isolates of the 123 urine cultures analyzed, specifically three *E. coli* one *K. pneumoniae*, *M. morganii* and *E. cloacae,* respectively. The AmpC betalactamase pattern was found in three isolates out of 123, specifically of *E. coli, K. pneumoniae* and *E. cloacae*. No resistance was observed with a carbapenemase producing K. pneumoniae pattern (KPC).

DISCUSSION

The main results of the study carried out in pregnant women with suspected UTI included a 29% prevalence of infection confirmed by urine culture. As far as the etiologic prevalence is concerned, there was a predominance of Gram negative bacteria, pri-

Figure 1.
Flow diagram of pregnant women included in the study on urinary tract infection in a Level III clinic in Medellín, Colombia, 2013-2015



marily *E. coli*, *K. pneumoniae* and *P. mirabilis*. Finally, significant resistance against trimethoprim-sulphamethoxazole, ampicillin-sulbactam, ciprofloxacin and cephalothin was found in the isolated bacteria. Extended spectrum betalactamases (ESBLs) as well as the AmpC type were also found.

When compared with the studies conducted in Colombia by Campo-Urbina in Barranquilla (12) and Gómez in Bogotá (13), the results of the latter show a lower frequency of 10.6% and 8.3%, respectively, than was found in this study. They all included a sample of pregnant women screened for urinary tract infection during prenatal care. The type of population studied could explain the difference in prevalence, considering that our study included patients with clinical suspicion of UTI, a fact that also explains the low frequency of pregnant women with asymptomatic bacteriuria. However, the findings are similar to those reported by Arroyave in Manizales (17), with a frequency of 31%

Table 1.
Sociodemographic and clinical characteristics of pregnant women with suspected urinary tract infection attending a clinic in Medellín, Colombia, 2013-2015

Characteristic	With (+) urine culture N=123	With (-) urine culture N=291
Age		
Median (IQR)*	24 (20-29)	26 (22-29)
Minimum-Maximum	13-42	15-44
Health insurance regime		
Contributive	103 (83.7)	255 (87.6)
Subsidized	11 (9.3)	24 (8.2)
Special	9 (7)	12 (4.1)
Number of pregnancies		
First pregnancy	62 (50.4)	126 (43.2)
Second pregnancy	38 (30.9)	104 (35.7)
Multiparous	23 (18.7)	61 (20.9)
Risk factors		
Kidney stones	11 (8.9)	13 (4.5)
Urinary tract malformation	6 (4.9)	6 (2.1)
Gestational diabetes	5 (4.1)	18 (6.2)
Steroid use	5 (4.1)	5 (1.7)
Gestational age		
First trimester	17 (13.8)	43 (14.8)
Second trimester	52 (42.3)	108 (37.1)
Third trimester	54 (43.9)	140 (48.1)

* Interquartile range

in a sample of 1429 pregnant women attending a primary care center for prenatal visits, although the diagnosis of UTI was made on the basis of the urinalysis and not a culture. Findings are also similar to those reported by Quiroga *et al.* in México (18), with a 37% frequency of urinary tract infection diagnosed by urine culture in a cohort of women selected by convenience sampling and followed since the first trimester for at least 4 months.

Regarding the type of urinary infection, our findings are different from those reported by Abarzúa *et al.* (19) in Chile, in a sample of positive urine cultures of pregnant women, showing predominance of asymptomatic bacteriuria (50.45%), followed by low UTI (38.7%) and, lastly, acute pyelonephritis (10.81%). As mentioned above, the patients in our study had symptoms of urinary tract infection, explaining the difference.

In terms of the etiologic prevalence, our findings are similar to those reported by Casas *et al.* (20) who describe that 90% of the isolates were *E. coli* in a sample of women with a positive urine

Table 2.
Etiologic prevalence in 123 pregnant women with symptomatic UTI in Medellín, Colombia, 2013-2015

Characteristic	Total N = 123 n (%)
Isolated germ	
E. coli	71 (57.7)
K. pneumoniae	14 (11.4)
S. saprophyticus	9 (7.3)
P. mirabillis	9 (7.3)
E. faecalis	7 (5.7)
S. agalactiae	3 (2.4)
E. cloacae	3 (2.4)
M. morganii	2 (1.6)
S. marscecens	1 (0.8)
S. aureus	1 (0.8)

culture during pregnancy, and to those of Schenkel in Brasil (21), who reports predominant *E. coli* isolates (75.4%), with the prevalence being higher during the first trimester of gestation. Ferreira *et al.* also report that the most frequently isolated germ in 50 pregnant women admitted due to UTI was *E. coli* (64%), followed by *K. pneumoniae* (11%), *Enterobacter cloacae* (7%), *Klebsiella oxitoca* (4%) and other germs (14%) (22).

As to changes in resistance profiles, Ferreira in 2005 (22) reported in Neiva 80% *E. coli* resistance to ampicillin, 72% to ampicillin-sulbactam, 69% to cephalothin, 54% to trimethoprim-sulphamethoxazole and 7% to ciprofloxacin. In 2006, Casas *et al.* (20) described in Popayán a prevalence of 58% resistance to ampicillin in pregnant women with UTI, with no findings of resistance to ceftazidime, ceftriaxone or cefotaxime, and a low resistance to nitrofurantoin, amoxicillin-clavulanate, gentamicin

Table 3.
Antibiotic resistance profiles of germs isolated in pregnant women with urinary tract infections attending a clinic in Medellín, Colombia, 2013-2015

Isolated germ	Drug resistance n (%) *								
	Trimethoprim-sulphamethoxazole	Ampicillin-sulbactam	Ciprofloxacin	Cephalothin	Nitrofurantoin	Ampicillin	Gentamicin	Aztreonam	Total
E. coli	22 (31 %)	18 (25 %)	15 (21 %)	11 (15 %)	4 (6 %)	5 (7 %)	5 (7 %)	1 (1 %)	71
K. pneumoniae	0	3 (21 %)	0	0	4 (29 %)	1 (7 %)	0	0	14
P. mirabillis	2 (22 %)	1 (11 %)	2 (22 %)	0	1 (11 %)	0	0	0	9
E. clocae	0	0	0	0	0	0	0	0	3**
M. morganii	0	0	0	0	1 (50 %)	0	0	0	2
S. marscecens	0	0	0	0	0	1 (100 %)	0	0	1

* Totals do not correspond to the sum because one pregnant woman could be simultaneously resistant to several antibiotics. Moreover, not all drugs that showed resistance are presented.

** One pregnant woman with resistance to fosfomycin.

and cefalexin. Gómez *et al.* (13), for the period 2013-2015, in a primary care center of a private insurance company in Bogotá, report 37% *E. coli* resistance to ampicillin, 10% to ampicillin-sulbactam, 23% to trimethoprim-sulphamethoxazole, and 11% to ciprofloxacin. In a study conducted in 2014 and 2015 in Barranquilla, Campo-Urbina *et al.* (12) report 33% resistance of *E. coli* to ampicillin and ampicillin-sulbactam, 66% to trimethoprim-sulphamethoxazole, and 16% to nitrofurantoin. This study shows higher resistance to ampicillin-sulbactam, trimethoprim-sulphamethoxazole, cephalothin and ciprofloxacin of germs that cause UTIs in pregnant women.

The main weakness of this study is the fact that it is based on past institutional records. On the other hand, having excluded only patients who were on antibiotics the day before admission to the hospital, the proportion of negative cultures could have increased. Also, there may be selection bias of more severely ill patients given that they were patients who required hospitalization and may not be representative of the general population. The strength lies in the substantial number of isolates achieved and the availability of the resistance profile.

CONCLUSIONS

The prevalence of UTIs in pregnant women with clinical suspicion of the infection was 29%. There is a high profile of resistance to trimethoprim-sulphamethoxazole, ampicillin-sulbactam and ciprofloxacin in the study population. Current population-based studies are needed for a better approach to the resistance of bacteria that cause UTIs in the community. On the other hand, the high resistance observed could lead to the suggestion of not including the exposed antibiotics in the local management guidelines of pregnant women with community-acquired UTIs.

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Diana Marcela Marín-Pineda: epidemiological advisor, data collection and analysis, drafting and final review of the manuscript.

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