

## Antibiotic sensitivity profile of bacteria in urinary tract infections

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### Abstract

**Background:** Urinary Tract Infections represent a frequent reason of ambulatory medical consult. The high and increasing percentages of antibiotic resistance represent a challenge for the physician treating them.

**Aim:** To obtain epidemiological information of the sensibility profile from bacteria isolated in urine cultures.

**Methods:** Between February and June of 2014, 602 urine culture samples were collected from different laboratories in the cities of San Pedro Sula and El Progreso, Honduras. The variables analyzed were sex, age and bacteria, antibiotics with higher sensibility and with higher resistance in urine culture. The Kirby Bauer method was used to determine the sensitivity and resistance profiles of each urine culture. A total of 47 antibiotics were used in all the laboratories. The variables were correlated to describe the resistance and sensibility profiles of the list of antibiotics.

**Results:** The bacteria isolated were *E. Coli* (70.4%), *Enterobacter spp* (7.8%), *Klebsiella spp* (6.3%), *Citrobacter spp* (6.1%), *Proteus spp* (2.8%), *Staphylococcus s spp* (2.7%), *Pseudomona aeruginosa* (1.8%), *Streptococcus spp* (1.2%), *Hafnia alveii* (0.3%), *Morganella morgagni* (0.2%), *Serratia marcescens* (0.2%), *Neisseria gonorrhoeae* (0.2%). From 602 samples, the general sensitivity reported was: fosfomicin (n=415, 68.9%), amikacin (n=412, 68.4%), nitrofurantoin (n=376, 62.4%), gentamicin (n=364, 60.4%) y ceftriaxone (n=307, 50%). The resistance for all the samples reported was as follows trimetoprim sulfametoxazole (n=302, 50.2%), ciprofloxacin (n=230, 38.2%), levofloxacin (n=221, 36.7%), norfloxacin (n=220, 36.5%) y amoxicilin+clavulanic acid (n=204, 33.9%).

**Conclusions:** The results in this research reveal that due to their good sensitivity profile, antibiotics like fosfomicin and nitrofurantoin can be a viable empiric therapy in patients with low urinary, or not complicated tract infection before using wide spectrum antibiotics, always personalizing according to the clinical state of the patient and trying to avoid the development of antibiotic resistance.

**Keywords:** Urinary tract infections, antimicrobials, bacteriuria, *E. coli*, urine culture, uropathogen.

**Date received:** January 25, 2016

**Date approved:** August 18, 2016

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**Abbreviations:** UTI, urinary tract infection; TMP-SMX, trimethoprim sulfamethoxazole; ESBL, extended spectrum beta-lactamases

**Conflict of Interest:** the authors declare no conflicts of interest.

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Urinary tract infections (UTIs) have represented, over time, a reason for consultation in all private and public health institutions worldwide. Due to its high prevalence and frequent inadequate use of antibiotics, it is necessary to determine the

most common causal agents, populations most affected and patterns of local sensitivity and resistance, to achieve better clinical results and to establish a better use of antibiotics.

UTIs usually occur in a variety of ways, depending on their chronological evolution or site of urinary tract infection, with clinical syndromes: asymptomatic bacteriuria, recurrent UTI, complicated UTI, UTI associated with bladder catheterization, acute cystitis and acute pyelonephritis.<sup>1</sup>

In the collection of published regional articles, results were found that show a wide difference between *Escherichia coli* and the rest of colonizing bacteria of the urinary tract. Of these, it is worth mentioning: *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterobacter spp*, *Enterococcus spp*, *Citrobacter*, *Pseudomonas aeruginosa*, *Staphylococcus saprophyticus*, streptococci, *Serratia sp*, *Acinetobacter spp*, amongst others.<sup>1-7</sup>

Pavón et al., in a study with 1256 patients in a third level hospital in Nicaragua, it was obtained 76.7% of *E. coli* isolates.<sup>2</sup> Delgado, meanwhile, had 340 samples in another hospital of the same category in Costa Rica, of which 56.1% corresponded to *E. coli*.<sup>3</sup> Rodríguez et al. They worked 32 samples at another hospital of the same level in Honduras and reported 76% of *E. coli*.<sup>4</sup> On the other hand, Castillo, with 20 samples in another hospital of the third level and in an asylum of disabled in Honduras, 50% of cases of *E. coli* were reported.<sup>5</sup> Figure 1 shows the comparison between the main isolates of the reviewed studies. This data is similar to those of other authors, such as Guevara et al., in which 71 samples showed that *E. coli* was present in 63.89% of the cases.<sup>6</sup>

The cases of UTI associated with bladder catheterization are closely related to the duration of bladder catheter use. The reported bacteria are usually the same cause in the other syndromes, with *E. coli* being the most frequently found germ and accompanied by *Klebsiella spp*, *Enterococcus spp*, *Proteus spp*, *Pseudomonas aeruginosa* and *Candida spp*.<sup>7</sup>

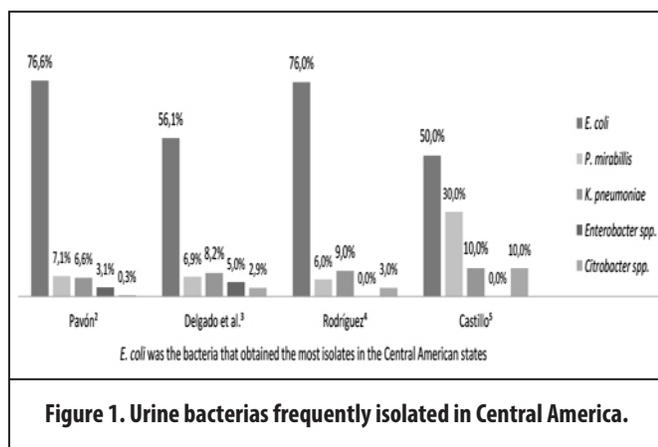


Figure 1. Urine bacteria frequently isolated in Central America.

The clinical context is also an important factor for the initiation of an antibiotic regimen, due to the susceptibility to UTI complications. Febrile infants, 2 to 24 months of age, should initiate treatment and change the therapeutic regimen by obtaining culture result according to specific patterns of sensitivity.<sup>8</sup>

The purpose of this study was to provide information regarding the bacteria frequently found as a cause of UTI and its patterns of sensitivity and resistance in the localities of San Pedro Sula and El Progreso, Honduras. This will help improve epidemiological surveillance of these phenomena. It is outside the scope of this study to delve into the characteristics of each pathology.

Nor is it intended to describe whether these bacteria were acquired in a hospital or community. It is extremely important to analyze the sensitivity and antibiotic resistance in urine cultures, since this diagnostic tool is used to provide specific medical treatment to patients with UTI. By having an analysis of an important sample of these exams, results that best refer to antibiotic susceptibility profiles can be obtained, which translates into results that could be of importance to orient the empirical therapy of UTIs when the urine culture is not available.

## Methods

This study is descriptive observational, transversal and retrospective.

The range of data collection included cities with high urban population density, so it was decided to take data from the different laboratories in the northwestern area of Honduras, which includes the cities of El Progreso and San Pedro Sula. San Pedro Sula is a part of the department

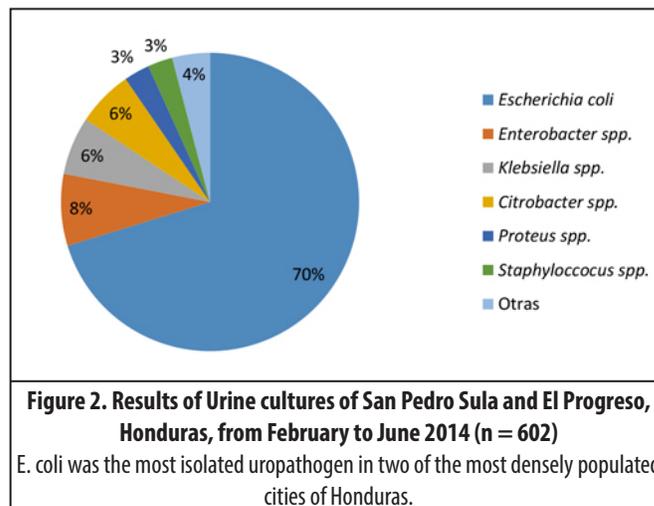


Figure 2. Results of Urine cultures of San Pedro Sula and El Progreso, Honduras, from February to June 2014 (n = 602)

*E. coli* was the most isolated uropathogen in two of the most densely populated cities of Honduras.

of Cortés, and the city of El Progreso is located in the department of Yoro.

The results of the urine cultures were obtained through different researchers in laboratories under strict norms of privacy and with the proper authorization of each institution source of the samples. A format was used for each researcher, created by the study coordinators.

The method used in all laboratories to obtain antibiotic resistance and sensitivity profiles was Kirby Bauer, with sensitivity disks. 47 sensitivity discs were used in all laboratories. Each researcher reviewed the database of Bueso Arias (San Pedro Sula), Fiallos (San Pedro Sula), UDE (El Progreso), Calix (El Progreso), Bendana Hospital (San Pedro Sula), Valle Hospital San Pedro Sula), Clinical Diagnostic Center (San Pedro Sula). After the complete collection, the analysis was performed by the researchers JZ and HV.

The inclusion criteria for the samples were: bacterial microbiological isolation obtained from urine samples of patients of any age, treated on an outpatient basis by public centers or in private consultation.

We included samples from participating laboratories without gender differentiation, including pregnant women.

Microbiological isolates positive for fungi or parasites were excluded from the analysis.

The variables from which data were collected were: age, sex, microorganism and antibiotic sensitivity test. The research protocol included origin (domicile), however, this variable was not analyzed, since almost no source provided such information.

Each variable was obtained from the database of laboratories that agreed to provide specific information, without jeopardizing privacy or exposing the name of each of the subjects in the study. No variable or other information was obtained externally from the assigned laboratories.

The samples were not placed in one or another category depending on any specific variable, which could affect the results in a positive way for the benefit of the study. The possible information bias includes the absence

<b>Table 1. General resistance of urine bacteria to antibiotics in the study</b>			
<b>Antibiotic</b>	<b>n (%)</b>	<b>Antibiotic</b>	<b>n (%)</b>
Trimethoprim sulfamethoxazole	302 (50,2)	Tetracycline	80 (13,3)
Ciprofloxacin	230 (38,2)	Nalidixic acid	65 (10,8)
Levofloxacin	221 (36,7)	Meropenem	45 (7,5)
Norfloxacin	220 (36,5)	Moxifloxacin	43 (7,1)
Amoxicillin + A. clavulanic	204 (33,9)	Amoxicillin	41 (6,8)
Cefixime	197 (32,7)	Amikacin	40 (6,6)
Cefuroxime	194 (32,2)	Clarithromycin	33 (5,5)
Cefaclor	191 (31,7)	Clindamycin	32 (5,3)
Ofloxacin	178 (29,6)	Ampicillin	28 (4,7)
Ampicillin + sulbactam	163 (27,1)	Oxacillin	20 (3,3)
Ceftriaxone	152 (25,2)	Penicillin	20 (3,3)
Cefadroxil	151 (25,1)	Enoxacin	18 (3)
Gentamicin	145 (24,1)	Erythromycin	10 (1,7)
Azithromycin	142 (23,6)	Mupirocin	10 (1,7)
Ceftazidime	125 (20,8)	Piperacillin + tazobactam	9 (1,5)
Kanamycin	121 (20,1)	Cefoxitin	7 (1,2)
Cephalexin	103 (17,1)	Dicloxacillin	7 (1,2)
Cefotaxime	101 (16,8)	Chloramphenicol	6 (1)
Fosfomicin	92 (15,3)	Imipenem	4 (0,7)
Aztreonam	91 (15,1)	Doxycycline	3 (0,5)
Nitrofurantoin	90 (15)	Cefoperazone	2 (0,3)
Tobramycin	83 (13,8)	Ampicillin + clavulanate	1 (0,2)
Cefepime	82 (13,6)	Cephalothin	1 (0,2)

of some antibiotic sensitivity discs, lacking results of other sensitive or resistant antimicrobials, which without altering the results, leaves out some antibiotics that could be resistant or sensitive than those presented in this study. It is also unknown if the samples came from patients with a primary infection, chronic infection, or if they had particular risk factors that could show different results.

A total of 602 samples were obtained and analyzed.

Quantitative variables were managed using coding. In the case of the age, in ranges of 10 years between 0 and 70. Regarding the antibiogram, the division of antibiotics was performed, to which the bacterium presented resistance, sensitivity and intermediate sensitivity.

All the results were sent to a data matrix in the program Microsoft Excel 2013<sup>®</sup>, to determine the percentages.

The study was carried out in line with good clinical practice, derived from the International Conference on Harmonization and the Helsinki Declaration. In addition, all existing laws were complied with. It was

approved by the institutional ethics committee and local authorities, before starting the study.

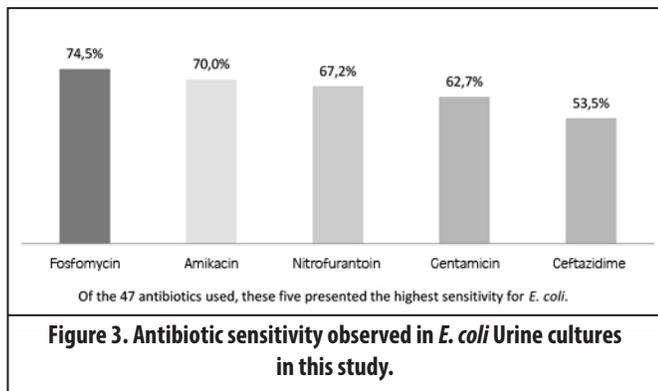
## Results

A total of 602 culture results were collected, of which 509 (84.6%) came from women and 93 (15.4%) from men. With respect to age, 84 samples (14%) belonged to individuals between 0-10 years old, 30 (5%) to cases between 11-20 years old, 260 (43%) between 21-60 years and 205 of the samples (34%) were for people over 61 years of age. No age data were obtained in 23 samples (4%) in which 18 were females and 5 males.

### Data generated

Of the 602 samples positive for bacteria in the urine culture, *Escherichia coli* was isolated in 70.4%, *Enterobacter spp.* in 7.8%, *Klebsiella spp.* in 6.3%, *Citrobacter spp.* in 6.1%, *Proteus spp.* in 2.8%, *Staphylococcus spp.* in 2.7%, *Pseudomonas aeruginosas* in 1.8%, *Streptococcus spp.* in 1.2%, *Hafnia alveii* in 0.3%, *Morganella morgagni* in 0.2%, *Serratia marcenscens* in 0.2% y *Neisseria gonorrhoeae*, in 0.2% (Figure 2).

<b>Antibiotic</b>	<b>n (%)</b>	<b>Antibiotic</b>	<b>n (%)</b>
Fosfomicin	415 (68,9)	Azithromycin	122 (20,3)
Amikacin	412 (68,4)	Cephalexin	98 (16,3)
Nitrofurantoin	376 (62,5)	Cefadroxil	76 (12,6)
Gentamicin	364 (60,5)	Kanamycin	71 (11,8)
Ceftriaxone	307 (51)	Nalidixic acid	64 (10,6)
Ciprofloxacin	273 (45,3)	Moxifloxacin	50 (8,3)
Cefixime	263 (43,7)	Piperacillin + tazobactam	49 (8,1)
Cefuroxime	258 (42,9)	Cefoxitin	30 (5,0)
Levofloxacin	256 (42,5)	Tetracycline	27 (4,5)
Ceftazidime	232 (38,5)	Chloramphenicol	21 (3,5)
Cefepime	230 (38,2)	Ampicillin	13 (2,2)
Meropenem	222 (36,9)	Enoxacin	13 (2,2)
Norfloxacin	214 (35,5)	Amoxicillin	12 (2)
Ampicillin + sulbactam	207 (34,4)	Vancomycin	11 (1,8)
Cefotaxime	198 (32,9)	Erythromycin	6 (1)
Cefaclor	194 (32,2)	Cephalothin	5 (0,8)
Ofloxacin	189 (31,4)	Dicloxacillin	3 (0,5)
Trimethoprim sulfamethoxazole	182 (30,2)	Doxycycline	2 (0,3)
Amoxicillin + a. clavulanic	171 (28,4)	Ampicillin + clavulanate	1 (0,2)
Aztreonam	165 (27,4)	Clindamycin	1 (0,2)
Tobramycin	164 (27,2)	Imipenem	1 (0,2)



A total of 47 discs were used to determine the resistance and sensitivity profiles in each bacterial isolation. Antibiotics with high percentages of resistance were: trimethoprim sulfamethoxazole (50%), followed by third-generation quinolones with similar percentages, ciprofloxacin (38.2%), levofloxacin (36.7%) and norfloxacin 36.5%). The most resistant antibiotic in this study was amoxicillin plus clavulanic acid (33.9%) (Table 1).

According to the sensitivity profiles, the most effective antibiotics were fosfomicin (68.9%), amikacin (68.4%), nitrofurantoin (62.5%), gentamicin (60.5%) and ceftriaxone (50.1%) (Table 2).

There was a clear difference between the number of women (n = 509) and men (n = 93), in the total of samples studied. The profiles of sensitivity and antibiotic resistance between men and women were similar to the general sensitivity. However, in men, resistance to some cephalosporins is greater, but not in women, where the same pattern is maintained as in general resistance (Table 3).

Patient ages were categorized into the following ranges of 0-20 years (n = 114), 21-60 years (n = 260), over 61 years (n = 205). The profiles were maintained in a similar way as reported, however, in the group of 0-20 years, it was shown that there is a sensitivity of 48% to cefuroxime. It should be noted that the percentages of resistance were higher in people in the group over 61 years (Table 4).

Taking into account that the *E. coli* bacterium was the one with the most isolates presented (n = 424) and the one that has been studied the most in the literature, the resistance pattern was analyzed independently. It was evidenced that this bacterium, in the isolates analyzed, had a sensitivity profile similar to that of general sensitivity. However, sensitivity to ceftazidime was found to be only 53.5% (Figure 3). It was also observed that *E. Coli* presented significant resistance to TMP-SMX and four third generation quinolones (Figure 4).

The profiles of the other bacteria that presented in this study with less frequency of isolation, showed the following. *Enterobacter spp* was isolated in 47 samples and presented a sensitivity profile similar to that of all isolates; But it was observed that the antibiotics to which it presented greater resistance were amoxicillin plus clavulanic acid, cefaclor and cefadroxil. On the other hand, *Klebsiella spp* (n=38) had a sensitivity profile with good sensitivity to ciprofloxacin. As for resistance, there was similar pattern to that presented with respect to *Enterobacter*. *Citrobacter spp* (n=37) had a resistance pattern that showed resistance to quinolones and several cephalosporins. Finally, *Proteus* (n=17), presented an important resistance pattern with antibiotics that did not appear in the previous reports (azithromycin and ampicillin + Sulbactam) (Table 5).

Gender	Women (n=509)		Men (n=93)			
	Antibiotic	n	%	Antibiotic	n	%
Sensitivity	Fosfomicin	361	70,9	Amikacin	256	50
	Amikacin	353	69,3	Fosfomicin	189	37,1
	Nitrofurantoin	328	64,4	Nitrofurantoin	174	34,1
	Gentamicin	319	62,6	Gentamicin	170	33,3
	Ceftriaxone	277	54,4	Ciprofloxacin	165	32,4
Resistance	Trimethoprim / sulfamethoxazole	256	42,5	Trimethoprim / sulfamethoxazole	46	49,4
	Ciprofloxacin	189	31,3	Cefixime	44	47,3
	Norfloxacin	179	29,7	Cefuroxime	43	46,2
	Levofloxacin	174	28,9	Ciprofloxacin	41	44
	Amoxicillin + clavulanic acid	165	27,4	Norfloxacin	41	44

**Table 4. Main patterns of sensitivity and antibiotic resistance by age, in urine cultures in the study (n = 579) \***

Age (years)	0-20 (n=114)			21-60 (n=260)			> 61 (n = 205)		
	Antibiotic	n	%	Antibiotic	n	%	Antibiotic	n	%
Sensitivity	Fosfomicin	78	68,4	Amikacin	190	73,1	Amikacin	155	69,8
	Gentamicin	72	63,2	Fosfomicin	179	68,8	Fosfomicin	143	69,8
	Cefixime	57	50	Nitrofurantoin	176	67,7	Nitrofurantoin	140	68,3
	Nitrofurantoin	57	50	Gentamicin	168	64,4	Gentamicin	118	57,6
	Cefuroxime	55	48,2	Ceftriaxone	142	54,6	Ceftriaxone	106	51,7
Resistance	Trimethoprim / sulfamethoxazole	53	46,5	Trimethoprim / sulfamethoxazole	130	50	Trimethoprim / sulfamethoxazole	111	54,1
	Amoxicillin + clavulanic acid	37	32,5	Ciprofloxacin	102	39,2	Ciprofloxacin	105	51,2
	Cefadroxil	32	28,1	Norfloxacin	101	38,8	Norfloxacin	103	50,2
	Ampicillin + sulbactam	31	27,2	Levofloxacin	96	34,6	Levofloxacin	90	43,9
	Cephalexin	29	25,4	Amoxicillin + clavulanic acid	89	34,2	Ofloxacin	86	42

## Discussion

Antibiotics such as fosfomicin and nitrofurantoin, in this study show a good sensitivity profile in the isolates of the urine cultures analyzed, suggesting that they are a good option for the empiric treatment of uncomplicated low UTIs, since they are oral drugs without good Renal penetration. It was also shown that antibiotics such as quinolones had a high resistance profile throughout all analyzes.

Amikacin showed good sensitivity profile throughout all the results, as has been reported by other authors.<sup>9-13</sup> Despite this, the antibiotic would not be used as empirical therapy for uncomplicated UTIs, but for the management of a UTI where there is a multiresistance towards the other antibiotics that could cause fewer adverse events. The quinolones had high percentages of resistance, which is important, since some authors in Latin America report a high resistance to quinolones,<sup>9-12,14-15</sup> while others, a good sensitivity,<sup>16</sup> which leads to think that at the moment of a possible

**Table 5. Main patterns of sensitivity and antibiotic resistance of other bacteria identified most frequently in the study**

Bacteria	Enterobacter spp. (N=47)			Klebsiella spp. (N = 38)			Citrobacter spp. (N = 37)			Proteus spp. (N = 17)		
	Antibiotic	n	%	Antibiotic	N	%	Antibiotic	n	%	Antibiotic	N	%
Sensitivity	Fosfomicin	32	68,1	Amikacin	28	73,7	Amikacin	32	86,5	Gentamicin	13	76,5
	Amikacin	31	66	Fosfomicin	28	73,7	Nitrofurantoin	31	83,8	Amikacin	12	70,6
	Gentamicin	29	61,7	Ceftriaxone	25	65,8	Fosfomicin	27	73	Ciprofloxacin	10	58,9
	Ceftriaxone	25	53,2	Ciprofloxacin	25	65,8	Ceftriaxone	25	67,7	Norfloxacin	10	58,9
	Nitrofurantoin	25	53,2	Gentamicin	24	63,2	Gentamicin	18	48,7	Levofloxacin	9	52,9
Resistance	Amoxicillin + clavulanic acid	32	68,1	Amoxicillin + clavulanic acid	17	44,7	Cefaclor	27	73	Trimethoprim / sulfamethoxazole	9	52,9
	Cefaclor	29	61,7	Trimethoprim / sulfamethoxazole	17	44,7	Cefadroxil	26	70,3	Nitrofurantoin	8	47,1
	Cefadroxil	28	59,6	Cefixime	13	34,2	Amoxicillin + clavulanic acid	25	67,6	Nalidixic acid	6	35,3
	Trimethoprim / sulfamethoxazole	23	48,9	Nitrofurantoin	13	34,2	Trimethoprim / sulfamethoxazole	24	64,9	Ampicillin + sulbactam	6	35,3
	Norfloxacin	16	34	Cefaclor	12	31,6	Cefixime, ciprofloxacin, norfloxacin, and ofloxacin	22	59,5	Azithromycin and fosfomicin	5	29,4

empirical therapy, the endemic profiles of each country should be taken into account.

Certain authors consider age as a factor of importance with respect to increased resistance. Resistance is proposed to increase in people older than 60 years compared to those of younger age, which is usually associated with the use of catheters and chronic diseases.<sup>17,18</sup> It is clear that in the study there was an interesting difference between age groups and resistance percentages. As the age group was higher, the percentages of resistance were also slightly higher.

The antibiotic with the highest percentages of resistance throughout the study was TMP-SMX, which is in agreement with other studies in Latin America where resistance to TMP-SMX is frequent.<sup>11-16,19-21</sup> However, it has also been reported in the region, some sensitivity to TMP-SMX in the urine cultures.<sup>9,22</sup>

It is important to mention that, over time, good sensitivity profiles for nitrofurantoin have been beginning to be reported, albeit with limited spectrum; This antibiotic has been referred by many authors with a sustained sensitivity above 70% and even 80%.<sup>3,10-12,14,20</sup> In addition to this pattern, some authors outline a low resistance profile for nitrofurantoin.<sup>13,15-16</sup> This provides an interesting profile at the time of selection as empirical therapy for the management of uncomplicated low UTIs, in order to obtain high referral rates. In the study it was evident that this antibiotic, throughout all the analysis groups, was always sensitive above 50%.

Despite the fact that due to the method used for the isolation of the bacteria, direct detection of strains possessing extended spectrum beta-lactamases (ESBL) or cAMP was not made, it is necessary to mention as the Enterobacteriaceae acquire resistance by the mentioned above, and somehow could be inferred if indeed they are strains with these characteristics. It is known that the Enterobacteriaceae positive for ESBL possess significant resistance to ampicillin, ampicillin-sulbactam, ceftriaxone, sulfamethoxazole trimethoprim and quinolones.<sup>9,14-17,23</sup> This is of paramount importance, since the study shows that most of the isolates had a significant resistance to the antibiotics mentioned above. Secondly, Enterobacteriaceae also demonstrate a significant phenotypic characteristic, such as beta-lactamase cAmp, which confers significant resistance to third-generation cephalosporins.<sup>17,13</sup>

It would be advisable to carry out more observational studies in all the zones of the country, in order to promote the development of a local guide directed to the ambulatory management of the urinary infections of a staggered form, based on the resistance patterns that have in the region, through comparative studies.

Padgett, et al., in the Hospital of Specialties of the Honduran Institute of Social Security, reported the evolution of resistance of *E. Coli* from 2006 to 2009, through the committee of prevention and control of nosocomial infections. There was a slight decrease in resistance to ciprofloxacin from 42% to 35%, and ceftriaxone from 47% to 31%.<sup>24</sup>

The development of epidemiological and pharmacological surveillance programs would provide a powerful tool to reduce levels of antibiotic resistance related to causes such as underdosing, inappropriate use of antibiotics, among others. It is proposed to develop local prospective studies to determine which antibiotics would be most useful on a regional basis. The results encourage more complex studies, determine that there are actually better treatment options and have a good therapeutic escalation regarding patient management.

One of the limitations of the study was that the sensitivity disks were not the same in all laboratories. We did not obtain the addresses of the patient's places of origin, which would have provided breadth with respect to which areas have a higher prevalence of certain bacteria or antibiotic resistance in the metropolitan area, to determine the heterogeneity of this area.

**Funds:** The financing of the study belonged to each participant researcher, for which it was stated that there was no conflict of interest.

**Acknowledgments:** to the reviewers of this article: Bárbara Bribiesca, MD, Monique Baudrit, MD and Daniel Bustos, MD; to those who provided results of urine cultures; to the laboratories Fiallos, Bueso Arias, UDE, Del Valle Hospital, Bendaña Hospital and Clinical Diagnostic Center, of the cities of San Pedro Sula and El Progreso, Honduras. For their logistical support to carry out the study and the data collection, the colleagues Ángel Martínez, Eylin Urbina, Eduardo Borjas, María Elena Chavarría, Heidy Fúnez, Osman Fuentes, Dilcia Lagos, Rocío Lagos, Fernando Paz, María Mandujano, Shirley Baiza and Saúl Paz.

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