



Susceptibilidad antimicrobiana de bacterias causantes de infecciones del tracto urinario en mujeres y niñas

Antimicrobial susceptibility of bacteria causing urinary infections in women and girls

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Palabras claves:

infección del tracto urinario; antibiótico; urocultivo; antibioticoterapia; resistencia bacteriana; betalactamasas de espectro extendido(BLEE).

Resumen

Introducción. La infección del tracto urinario forma parte del grupo de las infecciones más frecuentes en los seres humanos, por lo que se la considera un problema de salud pública al presentar altas tasas de incidencia y morbilidad en la población pediátrica y adulta en diferentes regiones del mundo, siendo la mayor causa de estas de origen bacteriano, por lo cual los tratamientos se basan en la antibioticoterapia. Sin embargo, con el paso de los años se ha observado a nivel global el fracaso en los tratamientos empíricos debido a la resistencia bacteriana, presentando mayor incidencia países subdesarrollados. **Objetivo.** Caracterizar las diferentes especies bacterianas causantes de infección del tracto urinario en mujeres que acuden a consulta en la Fundación Humanitaria Pablo Jaramillo Crespo durante el año 2022, además identificar al agente causal más común y su clasificación dependiendo de si estos presentan o no la enzima betalactamasa de espectro extendido (BLEE). **Metodología.** Estudio descriptivo de cohorte transversal, documental secundario de muestreo no probabilístico por cobertura total. **Resultados.** De 304 urocultivos positivos se identificó un 62.5% casos de infección del tracto urinario en mujeres adultas y 37.5% en niñas, presentándose a *Escherichia coli* como el agente etiológico más común 82.2%, seguido de *Proteus mirabilis* 11.5%, *Klebsiella pneumoniae* 1.6% y 4.7% de otros microorganismos gramnegativos. Un 11.5% de casos positivos para la presencia de BLEE, siendo *Escherichia coli* el agente etiológico con más casos positivos para este mecanismo de resistencia con un mayor número de casos en la población infantil siendo de 21 casos. **Conclusión.** EL agente etiológico más común causante de Infección del tracto urinario en la población de esta casa de salud es *Escherichia coli*, presentándose un mayor porcentaje de casos de betalactamasa de espectro extendido en la población infantil, lo que demuestra la importancia de realizar un urocultivo y antibiograma para plantear un correcto esquema de tratamiento en los pacientes y así evitar que los microorganismos generen mecanismos de resistencia bacteriana. **Área de estudio: Salud, Laboratorio clínico**

Keywords:

antibiotic urinary tract infection; urine; cultureantibiotic therapy; bacterial resistance; extended spectrum beta-lactamases (ESBL).

Abstract

Introduction. Urinary tract infection is one of the most frequent infections in humans, and is therefore considered a public health problem with high incidence and morbidity rates in the pediatric and adult population in different regions of the world, being the main cause of these infections of bacterial origin. , therefore the treatments are based on antibiotic therapy. However, over the years, the failure of empirical treatments due to bacterial resistance has been observed globally, with a higher incidence in underdeveloped countries. objective. Characterize the different bacterial agents that cause urinary tract infection in women who come for consultation at the Pablo Jaramillo Crespo Humanitarian Foundation during the year 2022, also identify the most common causal agent and its classification depending on whether or not they present the beta-lactamase enzyme ESBL extended spectrum. Methodology. Descriptive cross-sectional cohort study, secondary documentary study of non-probabilistic sampling by total coverage. Results. Of 304 positive urine cultures, 62.5% cases of urinary tract infection were identified in adult women and 37.5% in girls, with Escherichia coli as the most common etiologic agent 82.2%, followed by Proteus mirabilis 11.5%, Klebsiella pneumoniae 1.6% and 4.7% of other largely negative microorganisms. There were 11.5% of positive cases for the presence of ESBL, with Escherichia coli being the etiologic agent with the most positive cases for this mechanism of resistance, with a greater number of cases in the pediatric population (21 cases). Conclusion. The most common etiological agent causing urinary tract infection in the population of this health center is Escherichia coli, with a higher percentage of cases of extended-spectrum beta-lactamase in children, which demonstrates the importance of performing a urine culture and antibiogram in order to establish a correct treatment plan for patients and thus prevent microorganisms from generating bacterial resistance mechanisms.

Introduction

Urinary tract infection (UTI) is defined as the presence and proliferation of pathogenic microorganisms in the urinary tract, usually caused by bacteria. Clinical symptoms compatible with this may or may not be present. Although, they can also occur due to viruses, fungi or parasites. (1,2). UTIs can manifest asymptotically or symptomatically, affecting any part of the urinary system: the kidneys, the bladder and the urethra, the most common being those in the lower tract. (3) It is part of the group of most frequent infections in humans along with respiratory and gastrointestinal infections, which is why it is considered a public health problem that affects millions of people each year by presenting high incidence and morbidity rates in the pediatric and adult population in different regions of the world. (4).

Urinary tract infections are common in women and many have had an episode of this type of infection at least once in their lifetime. Morbidity is high, with Enterobacteria being the most common uropathogens, and the main one being *Escherichia coli*, the microorganism most frequently involved in these infections and the responsible agent in 65-80% of cases. Other common Gram-negative bacteria are *Proteus mirabilis*, *Klebsiella pneumoniae* and other Gram-negative bacilli. (5).

Antimicrobial resistance (AMR) is defined as the ability of a microorganism to neutralize and/or resist the effect of the antimicrobial at therapeutic doses, and may be natural or acquired. (6,7).

It is called natural resistance when all strains belonging to the same species are resistant to an antibiotic. On the other hand, acquired resistance appears as a consequence of defense mechanisms developed by microorganisms and may occur mutations in the nucleic acid base sequence of the bacteria, transmitting this information to its offspring and through the transmission of extrachromosomal genetic material from other bacteria (plasmids and transposons) (7,8).

Among the resistance mechanisms generated by bacteria, the production of enzymes such as β -lactamases stands out, which are the main cause of resistance to β -lactam antibiotics in Gram-negative bacteria. These enzymes are characterized because their function within the bacteria is to break the amide bond in the β -lactam ring, which makes β -lactam antibiotics harmless to bacteria. (9).

Beta-lactamases are differentiated by their resistance spectrum, thus having the extended spectrum (ESBL), which have been described mainly in strains of *Escherichia coli*, *Klebsiella* spp. and *Enterobacter* spp, although also in non-fermenting microorganisms such as *Pseudomonas aeruginosa*, which confers resistance to all β -lactam antibiotics with

the exception of carbapenems, cephamycins and combinations of β -lactams with β -lactamase inhibitors.(10,11).

Worldwide, in 2019 there were around five million deaths associated with multi-resistant bacteria(12).In underdeveloped countries there is a greater risk of developing bacterial resistance due to several factors, including: lack of regulation and control in the administration of antibiotics,poor adherence to treatment, over-the-counter and marketing of antibiotics without a prescription (approximately 78% of antibiotics)and poor health systems(13–15).

The World Health Organization in its 2014 Global Report on Surveillance of Antimicrobial Resistance, revealed high percentages of resistance to third-generation cephalosporins, mainly in *Escherichia coli* and *Klebsiella pneumoniae*, both in nosocomial infections and in community-acquired infections. In this context, the WHO estimates that in 2050 the continued increase in antimicrobial resistance will produce a relevant clinical-economic impact, with an estimated ten million deaths per year and a reduction in global gross domestic product of between 2% and 3.5%.(16).

In Latin America, there are several reports, where the reality is the same, various studies carried out in Colombia, Brazil and Peru, reveal the resistance in *Escherichia coli* For ampicillin, the highest percentage was found (approximately 60%), followed by nalidixic acid and trimethoprim-sulfamethoxazole (approximately 40%). In *Klebsiella spp.*, the frequency of resistance was lower with 23% for trimethoprim-sulfamethoxazole, 22% ampicillin-sulbactam, 19% cephalothin, 19% nitrofurantoin and 15% ciprofloxacin.(17,18).

In Ecuador, several studies conducted determined that the microorganism that most frequently occurs as the causal agent of urinary tract infections in women was *Escherichia coli*, followed by *Klebsiella spp.*, in addition to these in the bacterial resistance profiles it is recorded that It presents resistance rates to ampicillin >50%, trimethoprim-sulfamethoxazole >20%, ciprofloxacin 56.8%, gentamicin 19.4% and amikacin 3.6%(19–21).

Furthermore, the National Institute for Public Health Research (INSPI), in its report from the National Reference Center for Antimicrobial Resistance, reports resistance figures for *Escherichia coli* in urinary tract infections with very high values such as: resistance to ampicillin between 70.4 and 87.2%, ampicillin-sulbactam between 37.8 and 53.6%, trimethoprim-sulfamethoxazole between 52.7 and 70.8%, ciprofloxacin between 45.5 and 79.1% and gentamicin between 18.4% and 30.2%(22)Current information regarding the treatment of multi-resistant bacteria comes from observational studies and clinical trials conducted mostly in adults, and there is little information on the pediatric population.(23).

The present study aims to characterize the different bacterial agents that cause urinary tract infection in women who come to the Pablo Jaramillo Crespo Humanitarian Foundation for consultation, as well as to identify the most common causal agent in both girls and adults, and to classify them depending on whether or not they present the extended spectrum beta-lactamase (ESBL) enzyme that causes bacterial resistance, thereby providing important data to this institution and to the Cuenca population in order to make known the current reality regarding this health problem and in this way allow a new approach to the different treatment schemes used in medical practice.

Methodology

A retrospective, descriptive, cross-sectional cohort study was conducted using secondary documentation. Non-probabilistic sampling by total coverage was used, where the data were obtained from the database of the microbiology area of the laboratory of the Pablo Jaramillo Crespo Humanitarian Foundation in a period from January 2022 to December 2022.

Table 1.Type and level of research

According to its purpose	Basic	The most common microorganism causing infection may be determined during 2022
According to its scope	Retrospective.	Data obtained from urine cultures in 2022 will be analyzed
According to its depth	Descriptive, transversal	The study aims to explore labor performance in masonry sectors, no hypothesis is required.
According to their sources	Mixed	Primary and secondary sources will be used.
According to his character	Qualitative	The most common bacterial agent will be characterized, in addition to the presence of ESBL.
According to its nature	Non-experimental	Urine culture data was collected from the year 2022

The study population consisted of 750 female patients of all ages who underwent urine cultures during 2022, excluding male patients, as well as samples of any type other than urine, as well as growths with a count less than 5,000 CFU/mL. The sample consisted of 304 positive urine cultures obtained from isolates cultured on blood agar and McConkey agar with bacterial growth $\geq 50,000 - 100,000$ cfu/mL, of which their identification was carried out by means of identification schemes for microorganisms from Bergey's Manual of Systematic Bacteriology(24), and to determine antimicrobial susceptibility, the agar disk diffusion method established by Kirby and Bauber was performed, according to the recommendations of the Clinical and Laboratory Standards Institute, (CLSI, 2022). In

addition to the use of the broth microdilution technique with dehydrated AutoScan Beckman Coulter® panels, for identification of the microorganism, the minimum inhibitory concentration (MIC) and the presence or absence of ESBL. The data obtained were recorded in Microsoft Excel tables and subsequently analyzed using descriptive statistics in the SPSS program.

Within the study, compliance with the standards established in the Declaration of Helsinki Addendum of Taiwan was guaranteed, providing protection, privacy and confidentiality of the data collected, so that the physical and psychological integrity of the same was not attacked at any time. (25).

Results

Once the study is completed it was observed that out of a total of 750 urine cultures performed on women during the year 2022 at the Pablo Jaramillo Crespo Humanitarian Foundation, a total of 304 positive urine cultures were obtained, where the etiological agent that occurs in the highest percentage as a cause of urinary tract infections in women was *Escherichia coli* with a total of 250 cases representing 82.2%, followed by *Proteus mirabilis* 35 cases (11.5%) and *Klebsiella pneumoniae* 5 cases (1.6%), *Enterobacter cloacae* 4 cases (1.3%), *Citrobacter farmeri* 2 cases (0.7%), *Klebsiella aerogenes* 3 cases (1%), *Kluyvera ascorbata* 2 cases (0.7%), *Klebsiella oxytoca* 2 cases (0.7%) and *Pseudomonas aeruginosa* 1 case (0.3%) (Chart 1). 190 (62.5%) cases occurred in adult women and 114 (37.5%) in girls, being in non-pregnant women 153 cases (50.3%), in which these infections occurred more frequently in the adult population while in the population of pregnant women it was only 37 cases (12.2%).

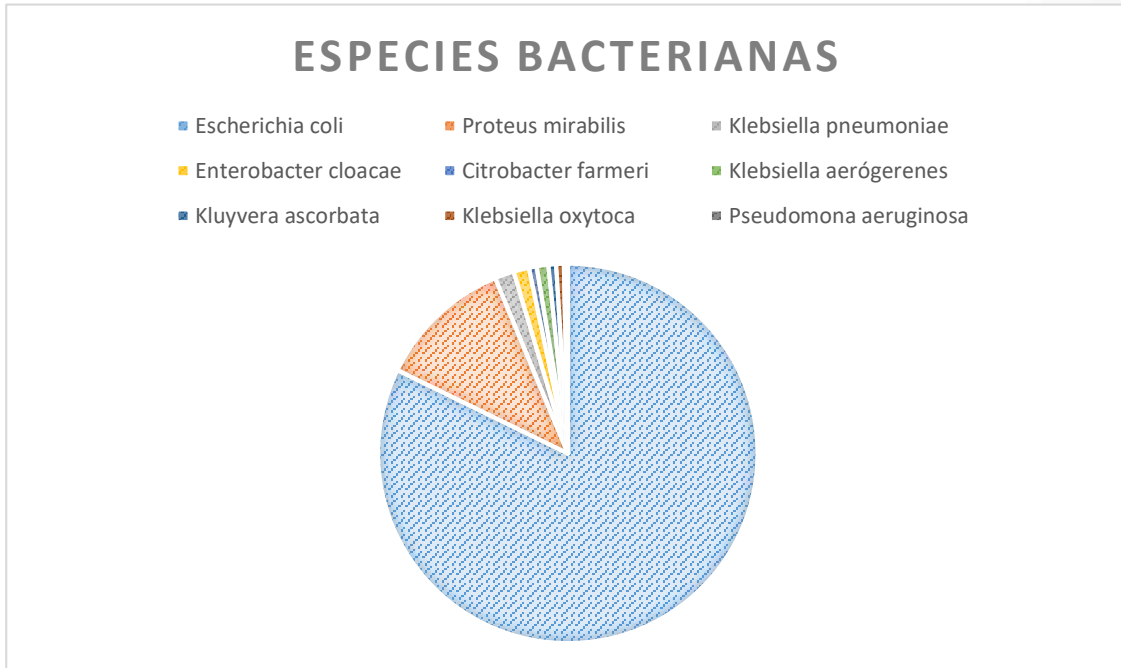


Chart 1 Bacterial species identified in the study population

Regarding the presence of ESBL, a total of 269 negative cultures were obtained and only 35 (11.5%) positive cases for this bacterial resistance mechanism (Table 2).

Table 2. Frequency of resistance mechanism (ESBL)

	<i>Frequency</i>	<i>Percentage</i>
BLEE	35	11.5
Negative	269	88.5
Total	304	100.0

Escherichia coli was identified as the etiological agent with the most ESBL positive cases (28) (Table 3), with the highest number of cases in the child population being 21 cases, while in the adult population there were 14 cases.

Table 3. Bacterial Species Relationship *Resistance Mechanism

Bacterial Species	Resistance Mechanism		Total
	BLEE	Negative	
<i>Escherichia coli</i>	28	222	250
<i>Proteus mirabilis</i>	0	35	35
<i>Klebsiella pneumoniae</i>	2	3	5
<i>Enterobacter cloacae</i>	2	2	4

Table 3.Bacterial Species Relationship *Resistance Mechanism (continued)

	Resistance Mechanism		
	BLEE	Negative	Total
<i>Citrobacter farmeri</i>	0	2	2
<i>Klebsiella aerogerenes</i>	2	1	3
<i>Kluyvera ascorbata</i>	0	2	2
<i>Klebsiella oxytoca</i>	1	1	2
<i>Pseudomona aeruginosa</i>	0	1	1
Total	35	269	304

Discussion

Urinary tract infections are a common health problem, which mostly affects women, since according to epidemiological data, more than 50% of women worldwide have suffered from them at some point in their lives.(26),since these have a greater predisposition to vaginal colonization by uropathogens, due to a greater propensity of bacteria to adhere to epithelial cells, suggesting a genetic determination.(27), according to the study carried out, the results obtained are not far from the global reality where out of 750 urine cultures performed, a total of 304 positive results were obtained in women and a total of 30 positive urine cultures in the male population that is treated in this health center, with which it can be observed that there is a very marked predominance of urinary infections in women..

According to studies carried out in the country, in the province of Azuay the etiological agent that is most prevalent is *Escherichia coli*, which is similar to the study carried out in this article since the same bacterial agent is presented as the main cause of urinary tract infections, being 82.2%.(19,28)Likewise, according to several reports of studies carried out in Latin America, *Escherichia coli* is presented as the most common uropathogen found in urine cultures reported as positive.(1,17,21,29).

In addition to *Escherichia coli*, other uropathogens were identified, such as *Proteus mirabilis* and *Klebsiella pneumoniae*, which according to authors describe these as common agents causing urinary tract infections in women and are usually of clinical interest since cases of bacteremia may occur in hospitalized and immunosuppressed patients.(30–34).

According to the data obtained in the present study regarding the population in which urinary tract infections predominate, it was shown that adult women exceed the 37.5% of girls by 62.5%. According to some authors, infections in this age group may be related to some factors such as the beginning of sexual activity.(26,35). Of this population, the results obtained regarding the percentage of pregnant women who presented infection

was 12.2%, although it is not a high figure that corresponds to a total of 37 women, this data must be taken into consideration since it is stated that pregnancy can be a factor that predisposes and increases the risk of presenting urinary tract infections, since physiological changes occur such as pH variation and the influx of progesterone, which decrease the tone of the urethral smooth muscle and the stasis of the genitourinary tract, increasing the probability of infection.(36).

Another highlight of this study is the determination of ESBL, where of the 304 positive cultures we found a total of 35 microorganisms that presented ESBL, with 21 cases in children (6.88%) and 14 in non-pregnant adult women, which could be corroborated with the chi-square analysis where it was demonstrated that there is a relationship between the data referring to the microorganism *Escherichia coli* and the presence of BLEE, which presents a very similar panorama at a global level, since there are studies in Spain on ESBL-producing Enterobacteriaceae in children in Spain shows a similar trend since the epidemiology of community urinary tract infections in children < 14 years was evaluated, where a prevalence of ESBL-producing Enterobacteriaceae of 3.2% was revealed. Another study in children under two years of age admitted for community-acquired febrile UTI between 2005 and 2014 showed a similar rate of 3.5%, somewhat lower than that described in another study that analyzed community-acquired UTIs. *Escherichia coli* in children under 14 years of age during 2015 and 2016 (9.2%)(23), another study conducted in Latin America revealed that 19 cases (3.5%) were identified, 16 of which corresponded to *Escherichia coli* in children under 2 years of age(37), which is alarming since the fact that this resistance mechanism is more prevalent in the child population of this population shows us that microorganisms can adapt to the environment and develop these resistance mechanisms.

Conclusions

- Based on the results obtained in the present study, it can be concluded that the most common microorganism causing UTI is *Escherichia coli*. At a global level, when compared with various studies at both national and international level, the results reflect this reality, presenting a high incidence in the female population.
- As an alarming fact, after processing the results obtained, it was observed that there were more cases of ESBL presence in the child population, with which it can be concluded that currently the need to carry out a correct approach to this type of infections, since it is necessary to know firsthand the causal agent of the infection in addition to its sensitivity to the different antibiotics used in the treatments and determine whether or not there is the presence of enzymes that confer resistance, in this way a correct treatment could be guaranteed to eradicate the pathogen and thus prevent that over time they can generate enzymes capable of inhibiting antibiotics even if they present beta-lactamase inhibitors since as the

years go by the bacteria continue to adapt to their environment to survive. In addition to the need to update the data regarding bacterial resistance in the different populations and raise awareness that antibiotics should not be used without a prescription since it has been normalized in such a way that these cases of bacterial resistance occur and with it the therapeutic failure when treating the infectious process.

- In addition, it is expected to contribute data to show the reality of the population and thus improve the care of patients who attend this health center, as well as encourage professionals in the area to carry out more studies in the city to achieve greater coverage of the reality experienced by the population regarding bacterial resistance.

Conflict of interest

The authors declare that they have no conflict of interest in the publication of the article.

Authors' contribution statement

The article must be accompanied by a note, which expresses the contribution of each author to the study carried out.

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