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Frequency of Resistance of BLEE-Producing *Escherichia Coli* to the Antibiotic Ciprofloxacin in Patients with Urinary Tract Infections at St. Lawrence General Hospital, 2017-2018

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ABSTRACT

Escherichia coli is one of the main etiological agents of urinary tract infections and its treatment has become more complicated over the years due to the emergence of resistant strains such as BLEE producers. The objective of this research was to determine the level of resistance of extended-spectrum beta-lactamase (BLEE)-producing *Escherichia coli* to ciprofloxacin in patients with urinary tract infections who attended the Medical Clinic service of the General Hospital of San Lorenzo, perod 2017-2018. The methodology used was the review of 1017 medical records corresponding to the period 2017-2018 of which 353 positive urine cultures were included and microbial susceptibility testing was performed. The results showed that the most frequently isolated microorganism in the two years was *Escherichia coli* 35% (year 2017) and 36% (year 2018), of the total *Escherichia coli* strains isolated 40% were BLEE-producing in 2017 and 35% in 2018. In BLEE-producing *Escherichia coli* resistance to ciprofloxacin was observed 83% in 2017 and 87% in 2018, non BLEE-producing strains a lower resistance of 33% and 60% in 2017 and 2018 respectively, resistance according to sex was 40% for female sex and 60% for male in 2017, while in 2018 presented higher resistance female sex being the same of 86% and in male sex of 14%. Greater resistance was observed in ages between 70 to 79 years for 2017 and between 60 to 69 years in 2018.

Keywords: Bacterial resistance, *Escherichia coli*, extended-spectrum beta-lactamases, urinary tract infections.

RESUMEN

El objetivo de esta investigación fue determinar nivel de resistencia de la *Escherichia coli* productora de betalactamasas de espectro extendido (BLEE) a la ciprofloxacina en pacientes con infecciones urinarias que acudieron al servicio de Clínica Médica del Hospital General de San Lorenzo, periodo 2017-2018. *Escherichia coli* es uno de los principales agentes etiológicos de infecciones del tracto urinario, su tratamiento se ha ido complicando con los años debido a la aparición de cepas resistentes como las productoras de BLEE. La metodología empleada fue la revisión de 1017 fichas médicas correspondientes al periodo 2017-2018 de las cuales se incluyeron 353 urocultivos positivos a las cuales se realizó pruebas de susceptibilidad microbiana. Los resultados mostraron que el microorganismo aislado con mayor frecuencia en los dos años fue *Escherichia coli* 35% (año 2017)

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y 36% (año 2018), del total de cepas de *Escherichia coli* aisladas el 40% eran productoras de BLEE en el 2017 y el 35% en el 2018. En *Escherichia coli* productora de BLEE se observó resistencia a ciprofloxacina del 83% en el 2017 y 87% en el 2018, las cepas no productoras de BLEE una resistencia menor, de 33% y 60% en el 2017 y 2018 respectivamente, la resistencia según el sexo fue del 40% para sexo femenino y 60% para masculino en el 2017, mientras que en el 2018 presentó mayor resistencia el sexo femenino siendo el mismo de un 86% y en el masculino del 14%. Se observó mayor resistencia en edades entre 70 a 79 para el 2017 y entre los 60 y 69 años en el año 2018.

Palabras claves: Resistencia bacteriana, *Escherichia coli*, Betalactamasas de espectro extendido, infecciones urinarias.

INTRODUCTION

A problem that has been increasing is the resistance to antibiotics because it puts at risk the survival of the human population, this phenomenon that humans will not be able to control, increasing epidemics and infections, is caused by mutations of pathogenic microorganisms, to resist the fight for antibiotics (1).

There are microorganisms that have an incredible ability to adapt to extreme conditions, being able to survive high temperatures, frost, extreme salinity, in the absence of oxygen, in the presence or absence of light, among other extreme conditions, while the human being may need an average of 20 years. Antibiotics have revolutionized medicine because they have saved the lives of millions of people, but when seeking approval of new antibiotics or antimicrobials, the process is very slow and costly, and can take time to recover the investment, and this often reduces the interest of manufacturers and investors (2, 3, 4).

Antibiotics, unlike other medicines, are used for short periods of time (7 to 10 days), unlike others that can be used for longer periods of time due to chronic diseases, and a problem that a few years ago increased concern was the lack of regulation of pharmacies or drugstores in the sale of these medicines. Due to the fact that microorganisms can resist the effects of antibiotherapy, it is a phenomenon that attracts the attention of modern science, and, in relation to this problem, the World Health Organization has pronounced, requesting countries to minimize this risk, since it is a world public health problem (2, 5).

According to the World Health Organization in its first global report in 2014, it stated that antibiotic resistance is a threat that has ceased to be a forecast for the future and is already a reality in all regions of the world that can affect anyone of any age in any country. Resistance, which occurs when bacteria undergo changes that cause antibiotics to stop working in people who need them to treat infections, is already a major health threat. Dr Keiji Fukuda, WHO Assistant Director-General for Health Security has said that in the absence of urgent and coordinated action by many stakeholders, the world is headed for a post-antibiotic era in which common infections and minor injuries that have been treatable for decades will once again become life-threatening (2).

According to the **MSP** and **BS** (2018) antibiotic resistance is today one of the greatest threats to global health, food security and development. An increasing number of infections are

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becoming more difficult to treat due to the loss of antibiotic efficacy, and antibiotic resistance is accelerated by the misuse and abuse of these drugs (5).

Urinary tract infection (UTI) is considered the presence and multiplication of microorganisms with invasion of adjacent tissues that are part of the genitourinary system. When there is a presence of bacteria in urine equal to or greater than 10^5 Colony Forming Units (CFU), it is called "bacteriuria"; some symptoms and clinical history such as dysuria, pollakiuria, abdominal or lumbar pain, associated or not with data of systemic inflammatory response, should consider the possibility of UTI (6).

The most frequent etiological agent of urinary tract infections is the bacterium *Escherichia coli* (*E. coli*), which is also associated with intestinal infections and others such as nosocomial pneumonias, cholecystitis, peritonitis, etc. The isolation of *E. coli* strains with extended-spectrum beta-lactamases (ESBL) both in the community and in the hospital has become a growing problem. Extended-spectrum beta-lactamases (ESBLs), also called extended-spectrum beta-lactamases (ESBLs), are enzymes produced by large negative bacilli, mainly enterobacteria, most frequently *E. coli* and *Klebsiella pneumoniae*. In addition to penicillin and first and second generation cephalosporins, they are capable of inactivating oxymino-cephalosporins and aztreonam (7).

MATERIAL AND METHODS

Cross-sectional descriptive study, conducted at the General Hospital of San Lorenzo where existing situations were observed and not provoked in the research, has a quantitative approach as it correlates data, based on the measurement and the variables analyzed by statistical methods.

The cases were patients with urinary tract infections from different areas, where the population sample focused on patients with positive urine culture for *E. coli* BLEE. The inclusion criteria were: patients aged 18 years and older who had clinical history in the General Hospital of San Lorenzo, and with positive urine culture in the records of that Hospital. Those records from 2017 and 2018 from the medical clinic area were selected, analyzing a total of 1017 records of men and women.

RESULTS

A total of 1017 records of urine culture samples processed at the Central Hospital of San Lorenzo were analyzed, being 400 from the year 2017 and 617 from the year 2018, the frequency of samples processed from Medical Clinic was 164 and 189 corresponding to the year 2017 and 2018 respectively. In total, they tested positive to microbial growth from a total of 108 patients, being 44 from 2017 and 64 from year 2018.

Of the cases that were positive for microbial growth, isolation of microorganisms was performed, managing to isolate *Escherichia coli, Candida Albicans, Klebsiella Pneumoniea* and others.

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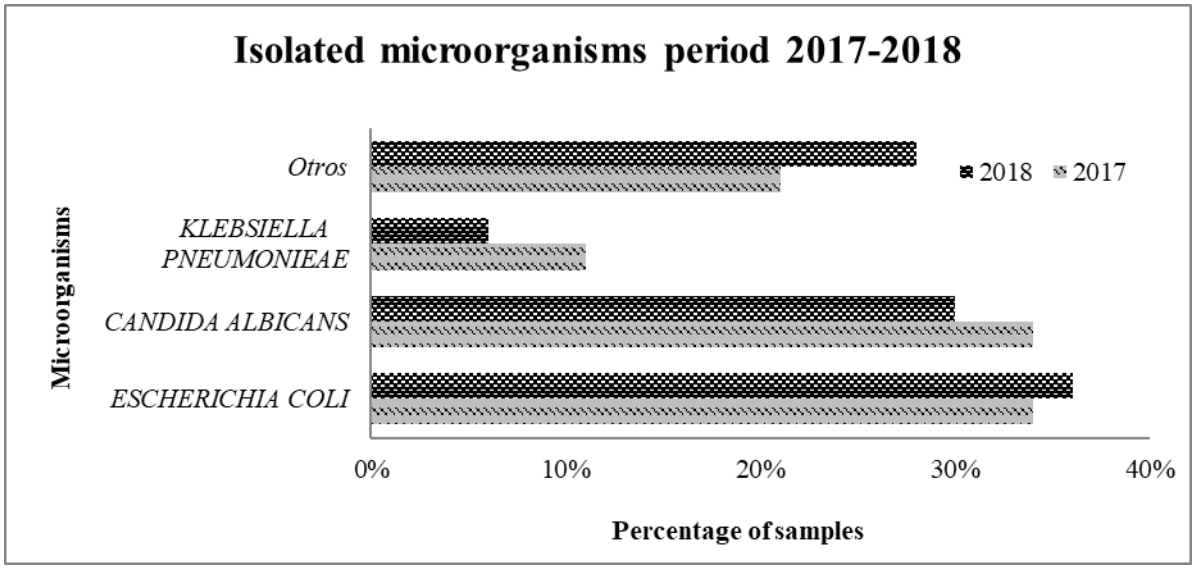

Figure 1. *Percentage of samples of microorganisms isolated during the period 2017-2018.*

Figure 1 shows the frequency of microorganisms isolated in urine culture samples that presented microbial growth in the laboratory of the General Hospital of San Lorenzo in the period 2017-2018. Of the total number of samples that presented microbial growth in 2017, it is observed that 34% of the samples correspond to *E. coli*, 34% *Candida albicans*, 7% *Klebsiella pneumoniae* and others in organisms with a percentage of 21% in 2018, of the total number of samples that presented microbial growth, it is observed that the highest percentage corresponds to *E. coli* with 36%, *Candida albicans* with 30% *Klebsiella pneumoniae* with 6% and with 28%. It is observed that, in both periods, the most frequently isolated bacterium in urine cultures was E. *coli.* From the analyzed data, the frequency of Betalactamase-producing and non-producing *E. coli*, processed in the laboratory of the General Hospital of San Lorenzo, was observed.

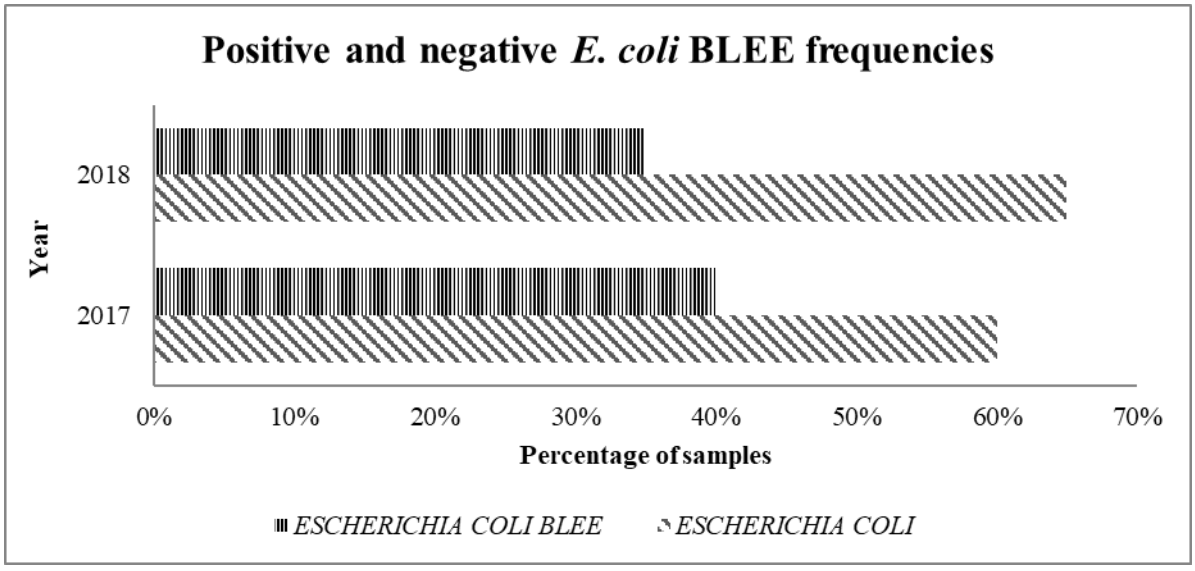

Figure 2. *Frequency of positive and negative E. coli BLEE.*

Figure 2 shows the frequency of *E. coli*, BLEE and positive. Of the total number of samples that tested positive for *E. coli* growth in the medical clinic area in 2017, 60% corresponded to non-

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BLEE-producing *E. coli* strains and 40% corresponded to BLEE-producing *E. coli* strains, while of the total number of samples that tested positive for *E. coli* growth in the medical clinic area in 2018, 65% corresponded to non-BLEE-producing *E. coli* strains and 35% corresponded to BLEE-producing *E. coli* strains. The frequency of sensitivity of BLEE-producing E. coli strains to ciprofloxacin can be seen in Figure 3.

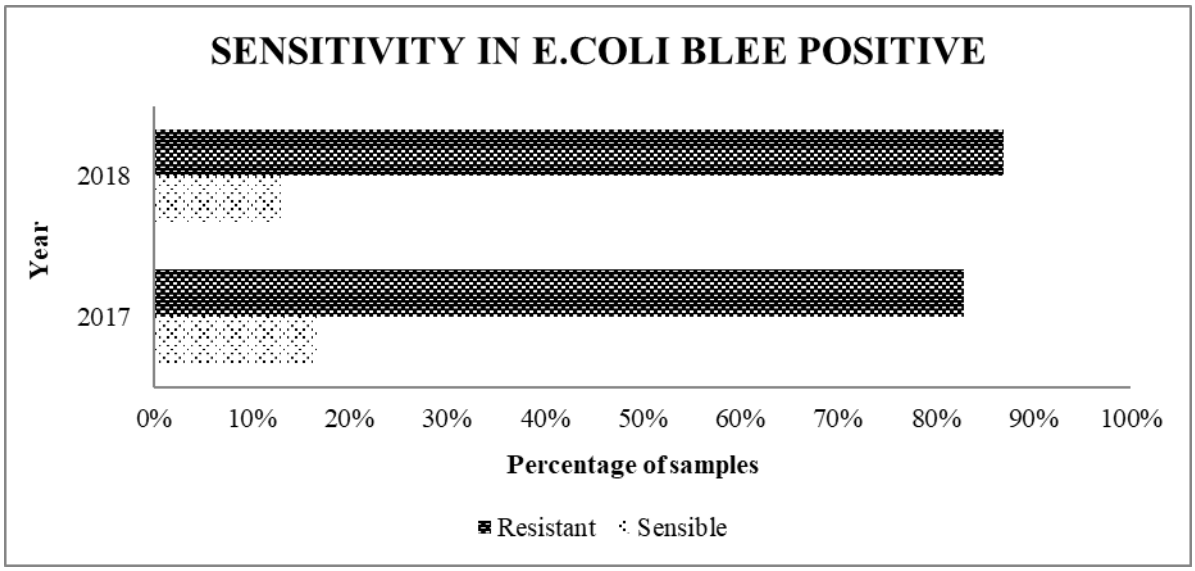

Figure 3. *Sensitivity in E. Coli Blee Positive*

Source: Data registry, obtained from clinical records of the General Hospital of San Lorenzo.

Figure 3 shows the percentage of samples that presented resistance to ciprofloxacin, in 2017. It can be observed that 83% presented resistance while 17% were sensitive to this drug. Of the total number of samples that tested positive for BLEE-producing *E. coli* in 2018, it can be observed that 87% presented resistance to ciprofloxacin, while 13% were sensitive to this drug. A high percentage of resistance to ciprofloxacin is observed in strains of *E. coli* producing extended-spectrum beta-lactamases.

DISCUSSION

One of the main causes of consultation in the hospital environment is urinary tract infection, the most frequent etiological agent is *Escherichia coli* with a frequency of approximately 85%, followed by other microorganisms such as *Proteus sp, Klebsiella pneumoniae, Enterococcus sp, Enterobacter sp*. (8, 9).

In the present study, the level of resistance of BLEE-producing *E. coli* to ciprofloxacin was determined, the most frequent etiological agent was *E. coli* and the production of beta-lactamases was observed in 40% of the cases. When enzyme-producing strains are present, they complicate the patient's treatment, making it longer and more difficult for the patient to comply with it.

The frequency of BLEE in E. coli was 37.5% on average, taking into account the data obtained in the years of study, above the data obtained by Cáceres Rojas et al. (2017), and Melgarejo, et. al. (2017), who found a frequency of 13% and 11% respectively, the closest being the one obtained by Leguizamón M., et al, (2017). which was 24.4% (10,11, 12).

Fluoroquinolones such as ciprofloxacin are usually the drugs of first choice for the treatment of urinary tract infections, however, this study found an increase in the levels of resistance in *E. coli* producer of BLEE to that antibiotic, with resistance of 83% in 2017 and 87% in 2018. Similar studies, such as that of Cáceres Rojas, et al, (2019), where they worked with similar microorganisms, observed a low resistance to ciprofloxacin, being the same of 27%.

The study of Gómez et al., 2009 obtained results where the percentage of resistance was 31.4%; on the other hand, Montañez-Valverde, et al. (2015) obtained percentages of resistance close to 70%, being the same of 69.8%; and Miranda (2013) stated that Colombia had a high percentage of resistance to ciprofloxacin by *E. coli BLEE,* with 76.6%. Through this analysis, it can be said that there is greater resistance to the antibiotic when it comes to *E. coli.* producer of BLEE, while percentage decreases when it is not of the same species (10, 13, 14).

CONCLUSIONS

The high resistance of BLEE-producing E. coli. suggests the need to provide other antibiotics for the treatment of urinary tract infections, where there is a predominance of the microorganism, because the treatment might not be effective by providing ciprofloxacin. The possible need to perform a resistance test to antibiotics that could be provided would be an alternative for a successful treatment. Likewise, the study should be expanded in order to have data and to know the regional and national reality about antibiotic resistance in patients with infectious conditions.

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