

2021

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Recommended Citation

Valero Román, Ítalo and Llanos-Tejada, Félix (2021) "Prior use of antibiotics and clinical characteristics of women who developed urinary tract infection due to beta-lactamase bacteria in a peruvian hospital," *Revista de la Facultad de Medicina Humana*: Vol. 21: Iss. 3, Article 11.

DOI: <https://doi.org/10.25176/RFMH.v21i3.3151>

Available at: <https://inicib.urp.edu.pe/rfmh/vol21/iss3/11>

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PRIOR USE OF ANTIBIOTICS AND CLINICAL CHARACTERISTICS OF WOMEN WHO DEVELOPED URINARY TRACT INFECTION DUE TO BETA-LACTAMASE BACTERIA IN A PERUVIAN HOSPITAL

USO PREVIO DE ANTIBIÓTICOS Y CARACTERÍSTICAS CLÍNICAS DE MUJERES QUE DESARROLLARON INFECCIÓN URINARIA POR BACTERIAS PRODUCTORAS DE BETALACTAMASAS EN UN HOSPITAL PERUANO

Ítalo Valero Román¹, Félix Llanos-Tejada^{1,a}

ABSTRACT

Introduction: The overused of antibiotics has existed as a threat to public health for several years. The World Health Organization (WHO) warns that in the year 2050 the "post-antibiotic era" will begin, where approximately 10 million deaths per year will be attributed to resistant infections. The infection where this type of bacteria is most relevant is in urinary tract pathology. **Objectives:** Determine the factors associated with the development of urinary tract infections by beta-lactamase-producing bacteria in older adults in the internal medicine service of the Dos de Mayo National Hospital. **Methods:** An analytical, cross-sectional, retrospective, case-control type study was carried out. Data were obtained through the review of medical records, with the completion of a data collection form related to sociodemographic aspects such as clinical data. With a total sample of 139 patients, 56 cases and 86 controls were obtained. To measure the association, we used the Odds Ratio, the statistical software SPSS was used. **Results:** A statistically significant association was observed between E. Coli ESBL infection with antecedents such as previous use of antibiotics and a history of recurrent urinary infection. The ORs and the confidence intervals of the variables that were shown to be significant were: recurrent urinary tract infection (95% CI, OR = 1,722), Anemia (95% CI OR = 1.96), Hypothyroidism (95% CI, OR = 1.13), Hypertension (95% CI, OR = 1,050), multi-pregnancy (95% CI, OR = 1,062) and History of previous antibiotic use (95% CI, OR = 22,106). **Conclusions:** The study identified the average age of presentation of urinary infection by E. Coli ESBL is between 65 to 75 years. Recurrent urinary tract infections and previous use of antibiotic treatment are significant risk factors for developing ESBL bacteria infections.

Key words: Urinary Tract Infections; beta-lactamase; Aged (source: MeSH NLM).

RESUMEN

Introducción: El uso indiscriminado de antibióticos existe como amenaza a la salud pública desde hace varios años. La Organización Mundial de la Salud (OMS), advierte que en el año 2050 comenzará la "era postantibiótica", donde se atribuirá a infecciones resistentes un aproximado de 10 millones de muerte por año. La infección donde se ve mayor relevancia este tipo de bacterias resistentes es la patología de vía urinaria. **Ojetivos:** Determinar los factores asociados al desarrollo de infecciones de vías urinarias por bacterias productoras de Betalactamasas en adultos mayores en el servicio de medicina interna del Hospital Nacional Dos de Mayo. **Métodos:** Se elaboró un estudio analítico, transversal, retrospectivo, tipo casos y controles. Se obtuvieron los datos a través de la revisión de historias clínicas, con el llenado de una ficha de recolección de datos relacionados a aspectos sociodemográficos como antecedentes clínicos. Con una muestra total de 139 pacientes, se obtuvieron 56 casos y 86 controles. Para medir la asociación, se utilizó los Odds Ratio para lo cual se usó el software estadístico SPSS. **Resultados:** Se observó una asociación estadísticamente significaba entre la infección por E. Coli BLEE con los antecedentes como el uso previo de antibióticos y el antecedente de infección urinaria recurrente. Los OR y los intervalos de confianza de las variables que mostraron ser significativas fueron: IVU recurrente (IC 95%, OR=1,722), Anemia (IC 95% OR= 1,96), Hipotiroidismo (IC 95%, OR=1,13), la HTA (IC 95%, OR=1,050), multigestación (IC 95%, OR=1,062) y Antecedente de uso previo antibiótico (IC 95%, OR=22.106). **Conclusión:** En el estudio se identificó que la edad promedio de presentación de infección urinaria por E. Coli BLEE se ubica entre los 65 a 75 años. Las infecciones urinarias recurrentes y el uso previo de tratamiento antibiótico son factores de riesgo significativos para desarrollar infecciones por bacterias BLEE.

Palabras clave: Infección urinaria; Beta lactamasa; Adulto mayor (fuente: DeCS BIREME).

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Cite as: Ítalo Valero Román, Félix Llanos-Tejada. Prior use of antibiotics and clinical characteristics of women who developed urinary tract infection due to beta-lactamase bacteria in a peruvian hospital. Rev. Fac. Med. Hum. July 2021; 21(3):540-545. DOI 10.25176/RFMH.v21i3.3151

Journal home page: <http://revistas.urp.edu.pe/index.php/RFMH>

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INTRODUCTION

The overuse of antibiotics has been seen before, accompanied by a lack of knowledge of the complications that lead to the excessive use of antibiotics, granting our ever present enemies, the pathogens, the capacity to develop immunity to commonly used antibiotics, leaving us without existing therapeutic measures⁽¹⁾.

The centers for disease control and prevention (CDC) warns over the diverse bacteria that develop resistance to multiple antibiotics due to its overuse, which leads to the decrease of therapeutic options and a greater difficulty in reaching patient recovery⁽²⁾. We emphasize that the indiscriminate overuse of antibiotics by humans is not the only cause, it is also reported that the use of livestock creates resistant bacteria. The most well-known resistant pathogens are methicillin-resistant staphylococcus aureus (MRSA), an extended spectrum beta-lactamase coliform producer, and the most feared are the carbapenem coliform producers⁽³⁾.

The World Health Organization (WHO) warns that in the year 2050, the "post-antibiotic era" will begin, where approximately 10 million deaths per year will be attributed to resistant infections⁽⁴⁾.

The infection with more relevance to this type of resistant bacteria is in the urinary tract pathology, which, during carbapenem coliform producers in most recent years, its incidence has increased with respect to antibiotic resistant bacteria, frequently presenting as Cystitis or Acute Pyelonephritis⁵. In several studies, a close relationship between prior infections treated with antibiotics and a greater risk of new infection by a pathogen resistant to standard treatments has been shown⁶. There are many published studies that ensure said phenomenon, however, many other non-assessed factors exist, such as sociodemographic characteristics.

Escherichia coli is still the common pathogen in urinary system infectious pathology, responsible for 75-90% of urinary tract infections⁽⁷⁾.

In a review by MEDLINE in 2014, they identified that over 30% of nosocomial infections are urinary tract infections⁽⁸⁾. A study performed in the capital of Peru reports that there is an elevated prevalence of self-medication in urban areas⁽⁹⁾.

METHODS

Study design

An analytical, cross-sectional, retrospective, case-control type study was carried out. Data were obtained through the review of medical records, with the completion of a data collection form related to sociodemographic aspects such as medical record.

Population and sample

The population was comprised of all adult patients over 65 years of age treated at the Hospital Nacional Dos de Mayo during the year 2018, with a total sample of 139 patients with urinary tract infections due to E.coli.

Cases: patients with E.coli ESBL positive urine culture.

Controls: patients with E.coli ESBL negative urine culture.

Exclusion criteria

Patients with an intercurrent disease that impedes the data collection. Additionally, incomplete medical records were excluded.

Variables

Through national and international literature review, the following variables were raised: sociodemographic factors (age, education level), pathological factors (history such as Diabetes mellitus, hypertension, anemia, prior urinary tract infections, presence of urinary tract stones) and history of medication use.

Procedure

A data collection sheet was used as an instrument. We created a data base in Excel software with the data recollected. This base was processed in the statistical program SPSS for its analysis.

Statistical analysis

We used the SPSS software for the statistical analysis and the graph development. We considered a level of significance of 95%. Frequency and descriptive statistical tables were used for its interpretation. Possible associations were analyzed through Odds Ratio (OR) measurements. Multiple regression logistic was used for the multivariate analysis.

RESULTS

Out of the 139 medical records reviewed pertaining to women admitted in the Hospital Nacional Dos de Mayo that were examined as part of the study, we obtained 56 cases and 83 controls. The cases (ESBL positive urine culture) represented 40.3% of the total sample.

With respect to general characteristics, the maximum age found was 99 years and the minimum was 65 years (which is the cutoff point given by the WHO to define an elderly adult). The average age (mean) was 73 years. The patients originated from the region of Lima in 87.1%.

The patients with complete grade school represent 31.7%, while 1.4% of patients had high school education.

Likewise, the comorbidities studied presented the following distribution: the presence of prior urinary tract infection episodes occurred in 44.6%. The presence of kidney stones was seen in 10.8% of patients. Hypothyroidism was found in 6.5% of patients. The number of patients categorized as multigestational (≥ 5 births) were 54% of patients. Diabetes mellitus was found in 46.8% of patients. Hypertension was seen in 43.9% of patients. See Table 1.

Table 1. Main medical history in patients treated in the internal medicine department of the Hospital Dos de mayo for urinary tract infection.

	Cases (ESBL+)		Controls (ESBL-)		Total	
	n	%	n	%		
Anemia*						
Yes	29	24%	29	24%	58	47.54%
No	20	16.39%	44	36.07%	64	52.46%
Multigestational						
Yes	46	33.09%	21	15.11%	67	48.20%
No	10	7.19%	62	44.60%	72	51.80%
Recurrent Urinary Tract Infection						
Yes	29	20.86%	33	23.74%	62	44.60%
No	27	19.42%	50	39.57%	77	55.40%
Diabetes Mellitus						
Yes	32	23.02%	33	23.74%	65	46.76%
No	24	17.27%	50	39.57%	74	53.24%
Prior use of Antibiotics						
Yes	46	68.66	21	31.34	67	48.20%
No	10.00	13.89	62	86.11	72	51.80%
Hypertension						
Yes	24	34.43%	37	60.66%	61	43.88%
No	32	41.03%	46	58.97%	78	56.12%

*In the anemia variable, 122 records were studied due to the existence of 17 lost data.



We observed a statistically significant association between infection due to E. Coli ESBL and the history, such as prior antibiotic use and recurrent urinary tract infection.

In a similar manner, the OR and confidence intervals of variables that presented significant differences between the group with E.coli ESBL and no ESBL are shown. These variables were: recurrent urinary

tract infection (CI 95%, OR=1,722), Anemia (CI 95% OR= 1.96), Hypothyroidism (CI 95%, OR=1.13), hypertension (CI 95%, OR=1.050), multigestational (CI 95%, OR=1.062) and history of prior antibiotic use (CI 95%, OR=22.106). Likewise, we observed that other variables that did not pose a risk between the groups with E.coli ESBL and no ESBL were kidney stones, diabetes (Table 2).

Table 2. Bivariate analysis of factors and the group of patients with E coli ESBL and non ESBL.

Associated factors	Percentage of patients with the factor	p-value	OR	IC95%
Anemia				
Yes	47.54%	0.105	1.974	0.982 - 3.969
No	52.46%			
Multigestational				
Yes	48.20%	0.944	1.027	0.495 - 2.128
No	51.80%			
Recurrent Urinary Tract Infecgion				
Yes	44.60%	0.044	1.702	0.903 - 1.878
No	55.40%			
Diabetes Mellitus				
Yes	46.76%	0.044	0.659	0.437 - 0.994
No	53.24%			
Prior use of antibiotics				
Yes	48.20%	0.000	13.581	5.839 - 31.588
No	51.80%			

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DISCUSSION

The present study has extreme relevance in the practical clinical field as well as theoretical field, thanks to this we have a better vision of the determinant principles that may be associated with the development of infections resistant to antibiotics, whose frequency is emerging in hospitals as well as in the community.¹⁰

In our study we found that the average age was 71 years, but having only studied an elderly adult population, it is not prudent to associate older age as a risk factor. Also, we should take in consideration that life expectancy estimated in Peru is 73 years

of age, which would help to understand why there were few patients over 80 years of age.

The multigestational variable in diverse studies has obtained high Odds Ratio values¹¹. According to our results obtained, we evidenced a 38.1% frequency of patient with multigestational history. The interrelation of a urinary tract infection due to ESBL in multigestational women was present in 20 cases. We obtained an OR of 1.027. The association is sustained in the anatomical changes of the genitourinary as a consequence of labor trauma. However, there is a larger quantity of multigestational women who presented infection due to E.Coli ESBL.

We found an association between history of a recurrent urinary tract infection and the presence of E.Coli ESBL (OR=1.302, CI 0.903 - 1.878). In various studies, it is described that this association is a consequence of E.coli virulence factors, such as its fimbria which are able to attach to transitional epithelia⁽¹²⁾. As we mentioned, the trauma caused by labor results in a deformity in the feminine urogenital system. Also, lets associate it to the fact that menopause implies an estrogen hormone deficit which induces a vaginal pH alteration, which changing provokes a variation in the flora towards a pathogenic one⁽⁷⁾.

We also found anemia as a comorbidity in the presence of urinary trat infection due to E.Coli ESBL (OR=1.974, CI: 0.982 - 3.969). Anemia was found in a total of 20 patients that had infection by ESBL. We noted that 36% of the studied sample did not present any alteration in the blood count. This could be due that the fact they are elderly adults, their immune cellular and humoral response is not as effective. Among the alterations reported with greater measure we found Neutrophilia (40.6%) and Leukocytosis (48.9%). Diverse studies find a Lastly, with respect to prior use of antibiotics, we found a statistically significant association in our sample, which is backed up by other studies. The use of antibiotics by self-medication is an elevated prevalence than in urban areas. Also, the inadequate use of antibiotics due to over prescription has an important relvelance⁽⁹⁾. This all implies that infection by ESBL bacteria does not necessarily occur in

patients hospitalized as was the standard. Our study presented the limitation of not being able to discern if the patient was taking antibiotics due to over-prescribing or in a self-medicating form.

Despite the obtained results, the literature gives importance to other factors, which may be more useful when suspecting infection by ESBL bacteria. As in the study by Muñaqui et al, where he describes an associated risk when there are several catheters in the urinary tract⁽¹³⁾.

We recommend that the professionals in the health department register the age of sexual relation onset, as well as contraceptive use, no matter the unemployment time, since it also represents an associated risk according to the literature. With respect to the methodological level, we recommend validating these results in other populations of the different hospitals of the country, as well as by different age groups.

The limitations of this study are based on the existence of medical records with a deficient completion of which do not cover the complete number of factors to evaluate.

CONCLUSION

In this study, we identified the average age of presentation of urinary tract infection by E.Coli ESBL between 65 and 75 years. We concluded that the recurrent urinary tract infections and prior use of antibiotic treatment are significant risk factors to develop infection due to ESBL bacteria.

Authorship contributions: The authors participated in the genesis of the idea, project design, data collection and interpretation, analysis of results and preparation of the manuscript of this research work.

Financing: Self-financed.

Interest conflict: The authors declare no conflict of interest.

Received: June 03, 2020

Approved: May 20, 2021

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