ANALYSIS OF THE USE OF BETA-LACTAM ANTIBIOTICS IN ADMINISTRATION AND COST IN A TYPE 2 HOSPITAL IN ECUADOR

1 MGs. VERÓNICA MERCEDES CANDO BRITO PhD
ORCID https://orcid.org/0000-0001-9290-8523

Faculty of Sciences Teaching-Researcher of the "Escuela Superior Politécnica de Chimborazo (ESPOCH)" Riobamba 060103, Ecuador.
e-mail: vcando@espoch.edu.ec
Research Group on Leishmaniasis and other Parasitosis in Ecuador-LEISHPAREC.
Chimborazo, Ecuador.

[2] MSc. SANDRA NOEMÍ ESCOBAR ARRIETA PhD.
ORCID https://orcid.org/0000-0002-3347-0282

Faculty of Sciences, Teacher-Researcher of the "Escuela Superior Politécnica de Chimborazo (ESPOCH)" Riobamba 060103, Ecuador.
e-mail: sa.escobar@espoch.edu.ec
Research Group on Technology and Pharmaceutical Care of Ecuador - GITAFEC.
Chimborazo, Ecuador.

[3] MSc. RAQUEL VIRGINIA COLCHA ORTIZ
ORCID https://orcid.org/ 0000-0002-3252-9158
Faculty of Business Administration Teacher-Researcher of the "Escuela Superior Politécnica de Chimborazo (ESPOCH)" Riobamba 060103, Ecuador.
e-mail: raquel.colcha@espoch.edu.ec.
Research Group “Socioeconomic Observatory of Region 3: ECOSR-1”.

[4] MSc. MARIA VERÓNICA ALBUJA LANDI
ORCID https://orcid.org/ 0000-0002-5959-1429
School of Mechanics "Escuela Superior Politécnica de Chimborazo (ESPOCH)" Riobamba 060103, Ecuador.
e-mail: maria.albuja@espoch.edu.ec

Abstract

Objective: to evaluate the rational use of beta-lactam antibiotics in Hospital Type 2, observing that the management of beta-lactam antibiotics is vital. **Methodology:** the study was carried out in two phases. In the first phase, information was collected from the hospital database, where 892 clinical histories were identified; once inclusion and exclusion criteria were considered, 93 accessible clinical histories were obtained. The data were tabulated and statistically processed in the second phase using the IBM SPSS Statistics 26 program. **Results:** Once the data were processed, the most frequently prescribed beta-lactam antibiotics were identified: ceftriaxone (47.9%), ampicillin plus sulbactam (20.2%), ceftazidime (9.2%), piperacillin

plus tazobactam (7.6%). It was determined that 93.54% of the prescriptions were not based on Ministry of Public Health (MOH) protocols. Seventy-five percent of the medical personnel were evaluated, and it was determined that there is a diversity of criteria at the time of prescribing to initiate antibiotic therapy. Most respondents (67%) answered correctly, while 33% answered incorrectly. **Conclusions**: The use of beta-lactam antibiotics at the hospital level is inadequate because therapeutic protocols for diagnoses in patients attending at the consultation level are not considered. **Recommendation**: It is recommended that a protocol for the rational use of antibiotics be developed to improve antibiotic management at the hospital level.

Keywords: rational use, beta-lactams, antibiotics, hospital.

Resumen

Objetivo: evaluar el uso racional de antibióticos betalactámicos en el Hospital Tipo 2 observándose que el manejo de antibióticos betalactámicos es de vital importancia. **Metodología:** el estudio se llevó a cabo en dos fases, en la primera se recolecto información de la base de datos del hospital, donde se identificó 892 historias clínicas; una vez considerándose criterios de inclusión y exclusión, se obtuvieron 93 historias clínicas accesibles. En la segunda fase, se tabularon y procesaron los datos estadísticamente utilizando el programa IBM SPSS Statistics 26. **Resultados:** Una vez procesados los datos se identificaron los antibióticos betalactámicos de mayor prescripción fueron: ceftriaxona (47,9%), ampicilina más sulbactam (20,2%), ceftazidime (9,2%), piperacilina más tazobactam (7,6%). Se determinó que el 93,54% de las prescripciones no se basaron en protocolos del Ministerio de Salud Pública (MSP). Se evaluó en un 75% al personal médico y se determinó que existe diversidad de criterios al momento de una prescripción para iniciar una terapia antibiótica. La mayoría de encuestados en un 67% respondió de manera correcta, mientras que el 33% lo hizo con desaciertos. **Conclusiones**: El uso de antibióticos betalactámicos a nivel hospitalario es inadecuado porque no se considera los protocolos terapéuticos para los diagnósticos en los pacientes que acuden a nivel de consulta. **Recomendación**: Se recomienda elaborar un

protocolo de uso racional de antibióticos para mejorar el manejo de antibióticos a nivel hospitalario.

Palabras clave: uso racional, betalactámicos, antibióticos, hospitalario.

Introduction

Beta-lactamases are enzymes that degrade the beta-lactam ring and act as natural resistance mechanisms in some bacteria. These enzymes were first identified in 1940 in a strain of ***E. coli*** (Salmin Martar et al.), and bacteria use these natural enzymes to compete for a niche with other microorganisms. However, since the widespread use of penicillin (1941), the first strains of resistance to *Staphylococcus began* to appear, with them the so-called penicillinases. This led to the creation of new antimicrobials with a broader spectrum and the beginning of the evolution of resistance mechanisms developed by bacteria to survive (Moisés, 2013).

International statistics report that between 12 and 40% of those admitted to hospital acquire intra-hospital infections and reach figures of up to 66%; for this reason, the use of antibiotics is a control issue since inappropriate use leads to the so-called drug-related problems (therapeutic failures) and adverse drug reactions, having as a final result a marked resistance to drug therapy (Perez et al., 2019: pp.1-17).

In terms of economics WHO agrees: It is important to highlight that the cost of medical care for patients with resistant infections is higher than care for patients with non-resistant infections; due to longer duration of illness, additional diagnostic tests, administration of more expensive drugs and prolonged hospitalizations with the use of more methods for diagnosis and control of the disease (Isaías et al., 2018: pp.762-770).

According to the Minimum Basic Data Set (MBDS), the number of deaths caused by multidrug-resistant bacteria in Europe is estimated at 25,000 per year, with Spain accounting for about 2,800 per year, above the European average (Sánchez, 2019, p.181).

In total antibiotic consumption and critical antibiotics of special monitoring (3rd and 4th generation cephalosporins), Spain is located below the European average (AEMPS, 2019). Nevertheless, treating these infections costs 1.5 billion euros per year in the European Union (EU) (AEMPS, 2019).

By comparison, the United Kingdom reported less than 25% resistance to third-generation cephalosporins for 5,303 *Klebsiella pneumoniae* and 30,218 *Escherichia coli* isolates (WHO, 2019).

It should be considered that about one-third to one-half of antibiotic prescriptions are for respiratory tract infections, followed by gastrointestinal and skin infections, among other additional conditions, being most of these viral infections there are antibiotic prescriptions that are made empirically, exceeding in various studies a 50% of cases (Gonzales et al., 2019: pp.145-151).

The most numerous family of "beta-lactam" antibiotics in clinical and in-hospital practice

represents a high demand due to their therapeutic efficacy against the most recurrent infectious pathologies, thanks to their broad spectrum of action against gram-negative bacilli and gram-positive cocci, except for methicillin-resistant *Staphylococcus*. Furthermore, beta-lactam tolerance is very good; only 10% of patients present true allergies. In addition, it represents low toxicity a *priori*, residing mainly in gastrointestinal problems (Gonzales et al., 2019: pp.145-151).

Thus, the present research was retrospective and aimed to study the rational use of beta-lactam antibiotics at the hospital level and identify drug-related problems, which is important information for the health sector.

Methods

The study was carried out in the internal medicine hospitalization service. The research was qualitative, deductive, cross-sectional and retrospective. The research design was non-experimental because the variables were not intentionally manipulated but were directly observed from January to June 2019. The study population was the medical records of patients hospitalized in the internal medicine service.

A total of 892 patients admitted to internal medicine were identified, of which 119 made up the sample, and only 93 medical records of patients hospitalized in the internal medicine service were accessed. Considering the inclusion criteria, patients between 17 and 80 years of age were hospitalized in the internal medicine service with antibiotic therapy including beta-lactams, patients with a hospital stay of more than 2 days and the medical staff working in the internal medicine service at the Hospital were considered.

Data collection techniques were considered in two phases: in the first phase, the data collection instruments were structured, validated and applied: medical history record sheet and knowledge test for medical personnel.

In order to prepare the instrument for collecting information from the clinical histories, a base was structured with different variables such as age, sex, pathology, antibiotic therapy, dosage, route of administration, frequency, treatment time, and complementary therapy.

The test consisted of closed multiple-choice questions based on scientific articles, professional criteria and applied knowledge of predisposing factors for the irrational use of beta-lactam antibiotics. The test was applied to 9 physicians to evaluate the knowledge and degree of inappropriate use of antibiotics.

In the second phase, the data were analyzed, tabulated and processed in the IBM SPSS Statistics 26 statistical program, allowing descriptive statistical analysis. To discuss the results, tables and figures were used to interpret, analyze and correlate the tabulated information.

Results

The results obtained based on data collected from medical records of patients treated at the Tena Hospital in the period January-June 2019 to determine the rational use of beta-lactam antibiotics and identify problems related to the drugs, in addition to the application of tests to assess the knowledge of the medical staff working in hospitalization. The data have been grouped in

frequency tables.

1.1. Characterization of the population

The following data correspond to the characterization by sex of patients who received antibiotic therapy in January-June 2019.

Table 1. Patients prescribed antibiotic therapy characterized by sex hospitalized.

SEX	***Frequency***	***Percentage***
Male	37	39.78
Female	56	60.22
Total	93	100

Source: Own elaboration, inpatient medical records, 2020.

Of the hospitalized patients who were prescribed and received antibiotic therapy, it was found that 60.22% were female, while 39.78% were male, which is related to data obtained in a study on the frequent prescription of antibiotics in the population and their differences by sex and age, which shows that the use of antibiotic therapy is most prevalent in female patients with 40.4%, followed by 33.5% in males (Serna et al., 2011: pp.236-244).

However, this prevalence may vary, as shown by a study conducted at the General Teaching Hospital "Dr. Enrique Cabrera" on the use of antimicrobials in the medical service, where it shows that the highest prevalence is in the male sex with 52.1%, followed by the female with 47.9%, although the gap is small, it is demonstrated that not always those who receive antibiotic therapy in greater demand belong to the female sex (Pereira, Aboy and Pulido, 2016, p.1).

1.2. Age of patients who received antibiotic therapy in the inpatient department.

Table 2. Frequency according to age in the period January-June 2019.

AGE OF PATIENTS (YEARS)	***Frequency***	***Percentage***
17-35	29	31.18
36-53	20	21.51
54-64	10	10.75
65-80	34	31.56
TOTAL	93	**100**

Source: Own elaboration from medical records of hospitalized patients

According to the data collected and inclusion criteria, it is shown that patients aged 17-80 years were hospitalized in the internal medicine service, resulting in a higher percentage of patients aged 65-80 years (31.56%), followed by patients aged 17-35 years (31.18%), 36-53 years (21.51%)

and lastly, patients aged 54-64 years (10.75%).

In turn, Villa et al. (2019) mention that 85.5% of patients admitted to the internal medicine service of a tertiary hospital are over 65 years of age, which agrees with the present study's data since it indicates that most adverse events occur between those ages. In Spain, the prevalence of infection in geriatric patients ranges between 5.8 and 38.5% (Blasco, 2007, p.27).

It is known that being an older age group, they are more susceptible to infections than other age groups, and this is due to the existence of various factors that favor them, whether extrinsic (high risk of nosocomial infections, poor conditions associated with hygiene, use of bladder or nasogastric tubes) or intrinsic (weakening of the immune system). Chronic diseases of the classical type, together with diseases of a degenerative nature, are gaining ground to the detriment of traditional infectious diseases (Ramos and Pinto, 2015: p.107).

1.3. Prevalent diseases

The most prevalent diseases identified in January-June 2019 are summarized in the following table.

1.3.1. Most prevalent pathologies in patients admitted to hospital.

Table 3. Frequency of pathologies in patients during the period January-June 2019.

GROUP OF PATHOLOGIES	*Frequency*	*Percentage*
Urogenital diseases	29	31.18
Respiratory tract diseases	26	27.96
Skin and tissue diseases subcutaneous	19	20.43
Gastrointestinal diseases	5	5.38
Other pathologies	14	15.05
	93	100.00

Source. Own elaboration from Hospital Medical History Data Collection Matrix.

Table 4. Frequency of pathology groups about age of patients admitted to the internal medicine service in January-June 2019.

PATHOLOGY GROUP	*17-35*	*36-53*	*54-64*	*65-80*	*TOTAL*
Diseases urogenital	7	8	10	4	29
	7,5%	8,6%	11%	4,3%	31,2%
Diseases of the respiratory tract	5	3	10	8	26
	5%	3,2%	10,7%	8,6%	28,0%
Diseases of skin and subcutaneous tissues	10	3	4	2	19
	10,7%	3,3%	4,4%	2,2%	20,4%
Gastrointestinal diseases	2	1	2	0	5
	2,2%	1,1%	2,2%	0 %	5,4%

Other pathologies	5	5	4	0	14
	5,4%	5,4%	4,4%	0 %	15,1%
TOTAL	29	20	30	14	93
	31,18%	21,5%	32,26%	15,06%	100,0%

Source: Own elaboration from Hospital Medical History Data Collection Matrix.

Urinary tract infections, which are framed within urogenital diseases, are the most recurrent infections, with a total of 31.4%, with a higher incidence in ages 54-64 years (11%) and 36-53 years (8.6%), followed by respiratory tract diseases with 28%, with a higher incidence in ages 54-64 years (10.7%) and 65-80 years (8.6%).

Urinary tract infections are considered one of the most common pathologies after respiratory infections and are mainly age-dependent, increasing with the onset of sexual life, with an annual incidence of up to 15% in adults aged > 30 years (Wurgaft, 2010: p. 629).

Medina and Castillo describe in their research that after a first episode of a UTI, 27% of women have a confirmed recurrence within the next 6 months, and 2.7% have a second recurrence within the same time. However, recurrence is less common than uncomplicated UTIs, with 9% of women and 5.7% of men having a second episode within 1 year (Medina and Castillo, 2019).

According to data exposed by INEC in Ecuador, one of the main causes of morbidity during 2019 was pneumonia of unspecified organisms, with a report of 29,066 cases among men and women, of which 7,566 belong to people > 54 years of age, one of the pathologies with a requirement of special monitoring with pharmacological treatment to ensure safety and joint efficacy in antibiotic therapy for patients (INEC, 2019).

N390: Urinary tract infections, unspecified T630:

Toxic snake effect

L039: Cellulitis of unspecified

site A419: Sepsis, unspecified

J1449: Chronic obstructive pulmonary disease, unspecified

Table 5. Chi-square test of the relationship between age and pathologies of patients diagnosed and treated in the hospitalization service.

Chi-square test			
	Value	***Df***	***Significance bilateral asymptotic***
Chi-square of Pearson	194,590a	174	.136
N of valid cases	93		
a. 208 boxes (99.0%) have expected a count of less than 5. The minimum expected count is .10			

Source: Own elaboration from Hospital Medical Records Data Collection Matrix. SPSS statistical program.

Null hypothesis (Ho): patient age is not associated with pathology.

Alternative hypothesis (Hi): patient age is associated with pathology.

Using a descriptive, inferential analysis about the variables of age and pathology of the patients admitted to internal medicine, applying the X2 test, observing an asymptotic significance between variables with p=.136 >0.05 so that the null hypothesis can be rejected.

1.4. Prescription antibiotics

Table 6. Beta-lactam antibiotics with the highest prescription in the hospitalization area in January-June 2019.

Therapeutic Sub-Group	***Generic Name***	***Pharmaceutical Form***	***Frequency***	***%***
Penicillins	Ampicillin + Sulbactam	Parenteral solid	24	20,2
	Oxacillin	Parenteral solid	1	0,8
	Benzathine penicillin	Parenteral solid	2	1,7
Cephalosporins	Ceftriaxone	Parenteral solid	57	47,9
	Ceftazidime	Parenteral solid	11	9,2
Carbapenemics	Imipenem +Cilastatin	Parenteral solid	1	0,8
	Piperaziline+ tazobactam	Parenteral solid	9	7,6
	Imipenem	Parenteral solid	14	0,8
		Total	119	100

Source: Own elaboration from Hospital Medical Records Data Collection Matrix.

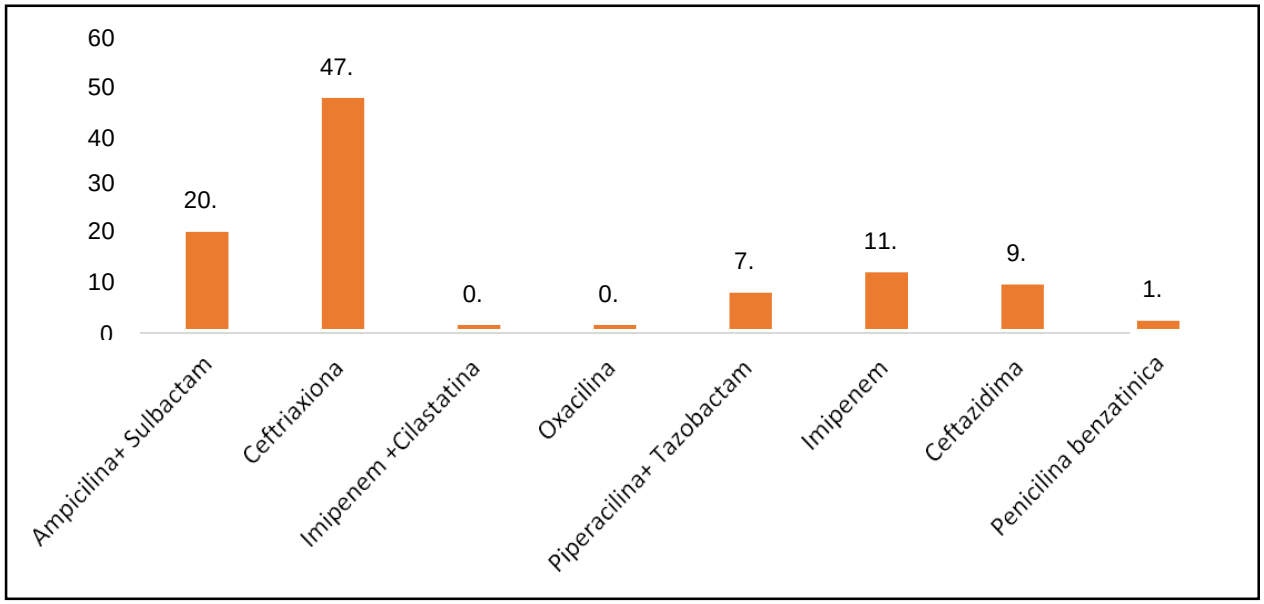

Figure 1. Most frequently prescribed antibiotics in patients admitted to the Hospitalization service in January-June 2019.

Source: Own elaboration.

The antibiotic with the highest prescription in the service is ceftriaxone, with a frequency of 57, followed by ampicillin + sulbactam with 24, and imipenem with 11.8. Ceftriaxone is one of the antibiotics that is mainly prescribed in hospitalization. This is reflected in consumption data according to a study conducted at the Clinical-Surgical Hospital "Comandante Manuel Fajardo" in 2016 with a frequency of 16,573 and 13,008 in 2017 respectively (Rojas et al., 2019: pp.9-14).

It should be noted that it is one of the first-line alternative antibiotics in treating urinary tract infections. Similarly, ceftriaxone or ampicillin +sulbactam are recommended pharmacological treatments for patients who have a stay < 7 days in hospitalization with pathologies caused by *Haemophilus influenzae*, *Streptococospneumonae*, (pneumonia of unspecified microorganisms) being these pathologies the most prevalent during the time of the study (Menéndez et al., 2019: pp.497-515).

1.4.1. Antibiotics prescribed per patient in the hospitalization service, in the period January-June 2019.

The antibiotic prescription to patients in internal medicine contained from one to 3 beta-lactam antibiotics as detailed below.

Table 7: Antibiotics prescribed by patients in the Hospitalization service for January-June 2019.

Beta-lactam antibiotics prescribed per patient	*Frequency*	*%*
UNO	70	75.27
TWO	20	21.51
THREE	3	3.23
TOTAL	93	100

Source: Own elaboration from Hospital Medical Records Data Collection Matrix.

According to data from patients admitted to the internal medicine department, 75.2% were prescribed one beta-lactam antibiotic in their treatment, 21.5% received two beta-lactam antibiotics, and 3.2% received three beta-lactam antibiotics. Drug combinations are common in treating infections caused by pathogens, such as e.g. multidrug-resistant Pseudomona aeruginosa, to broaden the spectrum, achieve antimicrobial synergy, improve therapeutic efficacy and prevent the emergence of resistance (Alvo et al., 2016: pp.136).

In turn, there was a coincidence with Peñaherrera, who mentions in his study: Use of antibacterials in the clinical area of the Hospital "José Carrasco Arteaga" the pharmacological treatment with 56.2% using only one antibiotic, 37.4 using two antibiotics and 6.4 using 3 antibiotics (Peñaherrera, 2013).

Table 8. Frequency of the type of pharmacological therapy received by patients in the hospitalization service for January-June 2019.

Type of Therapy	*Frequency*	*%*
Monotherapy	27	25,11
Combination therapy	66	61,38
Total	93	100

Source: Own elaboration from Hospital Medical Records Data Collection Matrix.

Of 93 patients hospitalized in internal medicine, 27 (25.11%) received monotherapy, while 66 (61.38%) received combined therapy in their pharmacological treatment. Monotherapy may be effective in early infections, but combination therapy is used as infections become recurrent and more aggressive.

Studies assessed the response rate to monotherapy, confirming that 30-35% of patients will respond to any drug in monotherapy and the rest will need combination therapy, while in other studies assessing the response rate to combination therapy with complementary drugs, these rates increase to 75-90%.

One factor that influences the response to treatment, on which the type of therapy will depend, is the evolutionary moment in which the patient is (Martell and Prieto, 2012: p.445).

1.4.2. Drug-drug interactions between beta-lactam antibiotics and other drugs.

Table 9. Drug-drug interactions in pharmacological therapy prescribed to patients in the hospitalization service for the period January-June 2019.

Drug interactions	***Frequency***	***Percentage***
Ceftriaxone + Amikacin	4	44
Ceftriaxone + Vancomycin	1	11
Ceftazidime+ Amikacin	1	11
Ceftriaxone+ Paracetamol	3	33
Total	9	100

Source: Own elaboration from Hospital Medical Records Data Collection Matrix.

Nine drug-drug interactions were obtained; most drug therapy has been combined mainly with aminoglycosides, to improve therapeutic efficacy, with greater empirical coverage with different agents and, therefore, a different spectrum of activity, added to the prevention or retardation of the emergence of bacterial resistance, however, several relevant aspects should be considered as possible adverse reactions, so it is important to control and monitor to avoid future complications, this association can affect between 10 to 20% of patients in renal failure (Martinez et al., 2016: pp.43-46).

Kuti (2016, p. 625) predicted that nephrotoxicity, ototoxicity, and neuromuscular blockade produced by using beta-lactam antibiotics and aminoglycosides such as gentamicin, tobramycin, or amikacin are significantly higher depending on the dose.

The combination of cephalosporins and nonsteroidal anti-inflammatory drugs (NSAIDs) is common to reduce inflation and pain; however, cephalosporins can be displaced from their plasma protein binding site when co-administered with an NSAID such as ibuprofen or paracetamol, which would result in a high plasma concentration of the antibiotic, this excess could result in tubular necrosis, other options should be considered, always identifying the antibiotic and NSAID to be administered (Flores et al., 2016: pp.227-234).

1.5 Correlation of pharmacological therapies according to Clinical Practice Guidelines and Protocols of the Ministry of Public Health.

Table 10. Correlation of clinical practice guidelines and protocols of the MOH in diagnosed pathologies of the hospitalization service in January-June 2019.

Use of clinical practice guidelines and MOH protocols				
GROUP OF PATHOLOGIES	***If you use*** **Frequency**	***%***	**Not used frequency**	**%**
Urogenital diseases	0	0	29	33,33
Respiratory tract diseases	1	10	25	28,74
Skin and tissue diseases subcutaneous	0	0	19	21,84
Gastrointestinal diseases	0	0	5	5,75
Other pathologies	5	90	9	10,34
Total	6 6,45	100	87 93,54	100 93

Source: Own elaboration from Hospital Medical Records Data Collection Matrix.

Knowledge of clinical guideline recommendations for antibiotic prescribing is the basis for appropriate prescribing; inadequate treatment can lead to erroneous prescriptions and a long hospital stay. However, some studies have shown that, generally, treatment guidelines for common infections are known and followed by physicians. The lack of treatment guidelines for some processes or their lack of updating may contribute to variability in some antibiotic treatments (Chamorro, 2019, p.5).

Based on the results, 93.54% did not prescribe pharmacological therapy according to clinical guidelines and protocols of the Ministry of Public Health; it should be noted that this state organization presents within its digital platform certain clinical guidelines for the treatment of recurrent pathologies as reported in the results, however, most of those described in the table is not found in guidelines of the MSP of Ecuador, with slight exceptions in clinical management guidelines and protocol for pathologies such as tuberculosis with 1.07% and the toxic effect of snake venom 5.34% (MSP, 2017).

The lack of adherence to clinical guidelines may be due to the non-existence of these guidelines in

the digital platforms of the MOH; however, there is evidence of similarity in pharmacological therapies with articles published in scientific journals, the knowledge that is applied in specific clinical cases such as the one with the highest incidence in the service: urinary tract infections that do not proceed in the same way for all, since most cases are treated with third-generation cephalosporins, when according to bibliography it mentions that to avoid superinfections and development of resistance, second-generation cephalosporins should be used for mild or moderate infections and restrict the use only for more severe infections to third generation cephalosporins and reserve ceftazidime to treat infections by *Pseudomonas* and other gram-negative bacilli resistant to other cephalosporins (Benedí and Raposo, 2005: p.52).

The lack of compliance with the correct use of clinical guidelines leads to therapeutic failures that generate bacterial resistance, which represents unnecessary resource expenditure.

Table 11. Chi-square test of the relationship between pathologies and therapeutic protocol of the MSP in patients diagnosed and treated in the hospitalization service.

Chi-square test			
	Value	Df	Asymptotic significance (bilateral)
Chi-square of Pearson	12,000[a]	4	,017
Likelihood ratio	13,171	4	,010
Linear association by linear	5,598	1	,018
N of valid cases	30		
a. 7 boxes (70.0%) have expected a count of less than 5. The minimum expected count is ,17.			

Source: Own elaboration from Hospital Medical Records Data Collection Matrix.

Null hypothesis (Ho): clinical diagnosis is unrelated to the therapeutic protocol.

Alternative hypothesis (Hi): clinical diagnosis relates to the therapeutic protocol.

Based on the descriptive, inferential analysis using the *X test*^{2}, a significant statistical relationship was observed between variables (pathologies and therapeutic protocol) with $p= 0.017 < 0.05$, demonstrating the acceptance of the null hypothesis since most of the pathologies were prescribed and treated with empirical pharmacological treatments not described in protocols and clinical guidelines of the MSP.

1.5. Knowledge of health professionals on the rational use of beta-lactam antibiotics in the hospitalization service.

The test was administered to resident physicians and specialists working in the hospitalization service, with a compliance rate of 75%, with 9 physicians being surveyed virtually, answering questions of professional and personal criteria on how to establish antibiotic treatment, in addition

to questions of knowledge on the use of a beta-lactam antibiotic.

The overall results of the survey are tabulated in tables and graphs.

Table 12. Frequency of medical staff criteria for using beta-lactam antibiotics in the internal medicine department of the HJMVI.

		F	**%**
Question. -1 When you are on this service, how often do you review your decision to prescribe antibiotics with a colleague?	Sometimes	3	33,3
	Most of the time	6	66,7
	Total	9	100
Question. - 2 How often do you agree with your colleague when prescribing antibiotic therapy?	Sometimes	2	22,2
	Most of the time	6	66,7
	Always	1	11,1
	Total	9	100

Source: Own elaboration from Hospital medical staff knowledge assessment test.

The prescription of drugs is a fundamental activity in the daily work of primary care physicians, who assume responsibility for the use of resources, the fact that a drug of high therapeutic value is consumed with greater demand is not synonymous with its correct use, so it is always important to discuss among professionals the appropriateness of applying an antibiotic treatment, always taking into account the effectiveness, safety and cost according to WHO in its Action Program on Essential Medicines (WHO, 2012).

66.67% admitted that they reviewed their prescription with a colleague. Likewise, 66.67% agree most of the time with their criteria for pharmacological prescribing therapy. In comparison, 22.22% agree sometimes, and 11.11% always agree, which reflects the similarity of criteria among the medical staff.

Figure 2. Question. -3 How often do you prescribe beta-lactam antibiotics in the internal medicine service?

Source: Own elaboration.

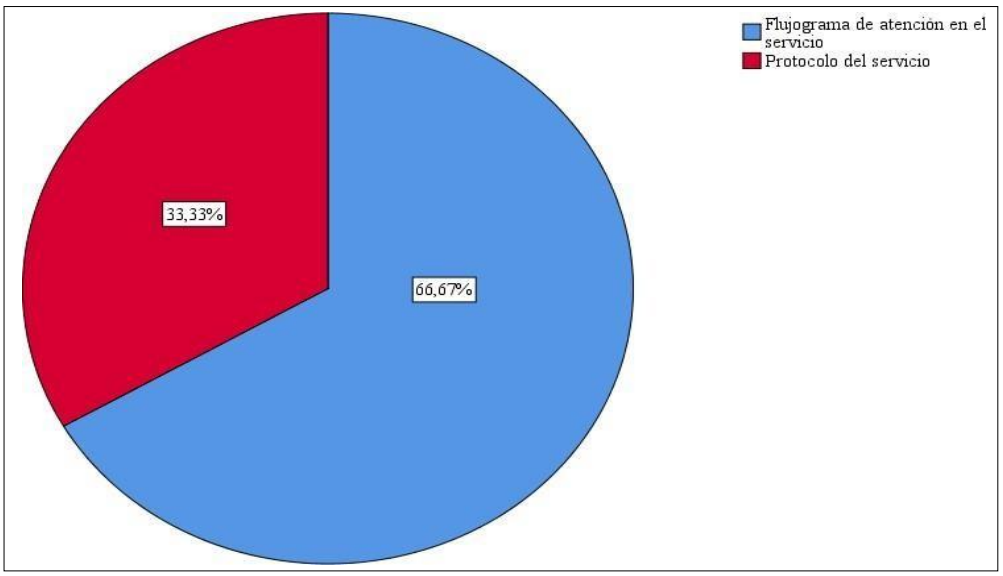

Figure 3. Question.4- On what basis do you make a decision when starting treatment?
Source: Own elaboration.

66.67% of the respondents stated that, for medical prescription, which initiates pharmacological therapy, they follow flowcharts of care in the service, while 33.33% follow service protocols; it should be noted that there may be confusion when interpreting a flowchart and protocol.

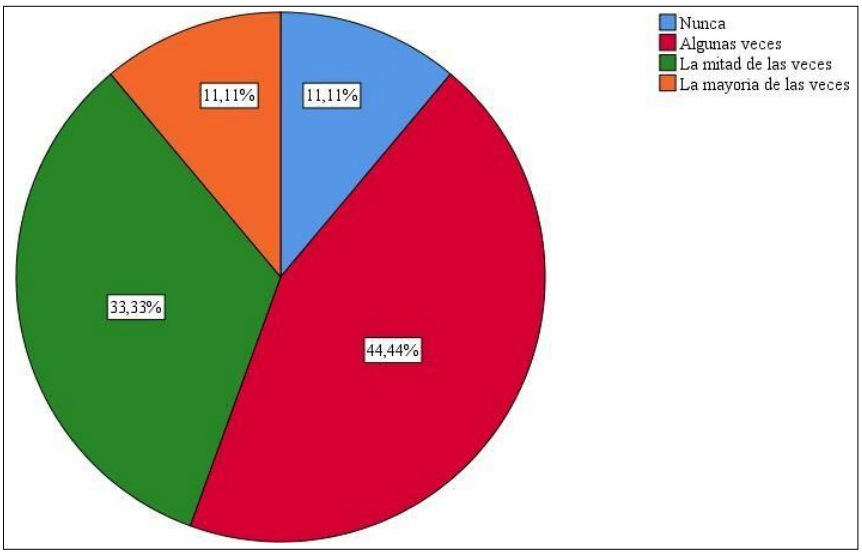

Figure 3. Question 5. How often do you request a microbiological culture to initiate treatment with beta-lactam antibiotics?

Source: Own elaboration.

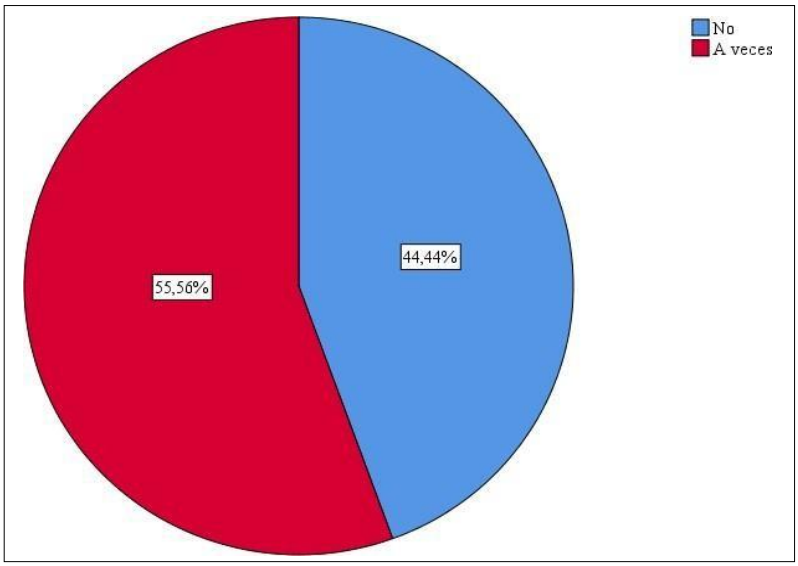

Figure 4. Question 6. In case the result of the microbiological culture is "no development," do you consider it pertinent to maintain the therapy with the prescribed drugs?

Source: Own elaboration.

Of the respondents, 44.44% confirmed that they sometimes request a culture to initiate antibiotic treatment; it is noteworthy that 11.11% never request a culture. 55.56% continue treatment despite not having microbiological culture results, while 44.44% change medication. Empirical treatment with broad-spectrum antibiotics continues to be initiated prophylactically and empirically until definitive microbiological information is available (Isaías et al., 2018: pp.762-770). This is justified by Zboromyrska et al. (2019) and colleagues, mentioning that the current recommendation is to prescribe empirical antibiotic treatment based on the pathology and its symptoms. In the case of complicated infections, the etiological spectrum is much broader, and the causative agents present greater resistance to the usual antibiotics, so the performance of a culture medium contributes to the optimization of treatment.

Table 13. Frequency of drug-drug interactions with beta-lactam antibiotics leading to decreased half-life and potentiation of nephrotoxicity.

What combination of drugs produces a shortened lifespan? and potentiation of nephrotoxicity?	*Frequency*	*%*
Imipenem+ Fenobarbitral	1	11.1
Ceftriaxone+ Amikacin	7	77.8
Ceftazime+ Keterolac	1	11.1
Total	9	100

Source: Own elaboration from Hospital medical staff knowledge assessment test.

77.78% mentioned an interaction between ceftriaxone + Amikacin which decreases the half-life between drugs and increases nephrotoxicity, while 11.11% indicated that the interacting drugs are Imipenem+ Phenobarbitral and Ceftazidime+ Keterolac respectively.

The existing interaction between beta-lactams and aminoglycosides potentiates nephrotoxicity and ototoxicity (Kuti, 2016, p.630).

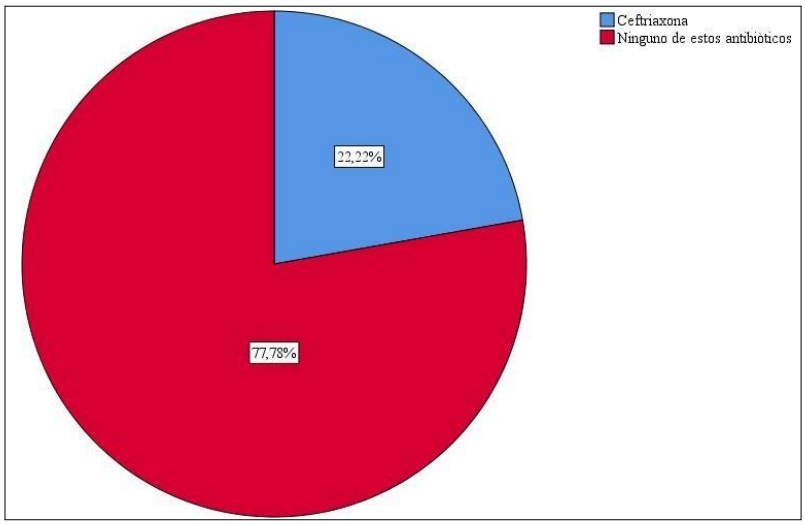

Figure 5. Question 7. If methicillin-resistant *Staphylococcus aureus* is susceptible to:
Source: Own elaboration.

Within the antibiotics cephalothin, cefuroxime, and ceftriaxone, 22.22% of the respondents state that ceftriaxone is susceptible to methicillin-resistant *Staphylococcus aureus*, while 77.78% rule out the aforementioned antibiotics.

Strains resistant to oxacillin and methicillin are historically referred to as methicillin-resistant *Staphylococcus aureus* (MRSA), are resistant to all ß-lactam agents, including cephalosporins and carbapenems, although they may be susceptible to the newer class of cephalosporins active against MRSA (Ceftaroline) (CDC, 2019).

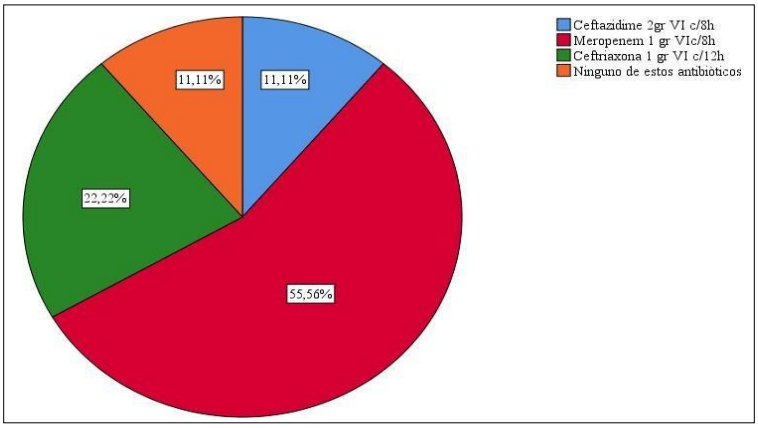

Figure 6. Question. A patient is admitted to the internal medicine service with a high urinary tract infection diagnosis and risk of BLEE-producing uropathogens. Which beta-lactam antibiotic of the first choice does he receive?
Source: Own elaboration.

55.56% of the respondents stated that meropenem 1g VI c/8h is used as the first-line drug for a high urinary tract infection with a risk of BLEE-producing uropathogens, 22.22% chose ceftriaxone 1g VI c/12h, 11.11% chose ceftazidime 2g VI c/8h and 11.11% chose none of these antibiotics.
BLEE are β-lactamases capable of conferring bacterial resistance to penicillins; first, second and third generation cephalosporins; and aztreonam (but not cephamycins or carbapenemics) by hydrolysis of these antibiotics, and which are inhibited by β-lactamase inhibitors such as clavulanic acid. Carbapenemics are the treatment of choice for severe infections due to BLEE-producing organisms (Rawat and Nair, 2010: p.263).

References

1. SALIM MÁTTAR ET. AL. Emergencia de la resistencia antibiótica debida a las β-lactamasas de espectro extendido (BLEE): detección, impacto clínico y epidemiología. Infectio 2007; 11(1):

23-35.

2. MOISES MOREJÓN GARCÍA. Betalactamasas de espectro extendido. Revista Cubana de Medicina. 2013;52(4):272-280

3. SÁNCHEZ, A. "Uso, abuso y mal uso de los antibióticos". Revista Enfermería CyL,[en línea], 2019 (11), pp. 181-188. [Consulta: 19 enero 2023]. Disponible en: http://www.revistaenfermeriacyl.com/index.php/revistaenfermeriacyl/article/view/240.

4. ISAÍAS, J., et al. "Prescripción racional de antibióticos: una conducta urgente". Medicina Interna de México [en línea], 2018, (México) 34(5), pp. 762-770. [Consulta: 19 enero 20231]. ISSN 0186-4866. Disponible en: http://www.scielo.org.mx/pdf/mim/v34n5/0186-4866-mim-34-05- 762.pdf

5. AEMPS. *Plan Nacional Frente a la Resistencia a los Antibióticos 2019-2021* [en línea]. Madrid- España: Agencia Española de Medicamentos y Productos Sanitarios, 2019. [Consulta: 19 enero 20231]. Disponible en: http://resistenciaantibioticos.es/es/system/files/field/files/pran_2019-2021_0.pdf?file=1&type=node&id=497&force=0.

6. OMS. *Antimicrobial steward ship programmes in health care facilities in low and middle in come countries a who practical Toolkit Antimicrobial Stewardship.* [en línea]. World Health Organization, 2019. [Consulta: 20 enero 2023]. Disponible en: https://apps.who.int/iris/handle/10665/329404

7. GONZÁLES, J., et al. "La resistencia a los antibióticos: un problema muy serio". Acta Medica peruana [en línea], 2019, (Perú) 36(2), pp. 145-151. [19 enero 20231]. ISSN 1018- 8800. Disponible en: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1728-59172019000200011

8. SERNA, C., et al. "Alta exposición a antibióticos en la población y sus diferencias por género yedad". Atención Primaria [en línea], 2011 (43), pp. 236-244. [Consulta: 2 febrero 2021]. ISSN 0212-6567. Disponible en: http://www.elsevier.es/es-revista-atencion-primaria-27-articulo-alta-exposicion-antibioticos-poblacion-sus-S0212656710003914.

9. PEREIRA, E., et al. "Uso de antimicrobianos en el servicio de medicina. Hospital General Docente Dr. Enrique Cabrera". Revista Habanera de Ciencias Médicas 2016 [en línea]. 2016. [Consulta: 19 enero 20231]. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1729-519X2016000300006.

10. RAMOS, P. & PINTO, J. "Health status of the elderly". Avances en Odontoestomatologia [enlínea], 2015 (31), pp. 107-116. [Consulta: 19 enero 2023]. ISSN 0213-1285. Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213-12852015000300001&lng=es&nrm=iso&tlng=es.

11. BLASCO, A. "Infections in nursing homes: The most frequent microorganisms, antimicrobial use and bacterial resistance". Revista Española de Geriatria y Gerontologia [en línea], 2007, (Vitoria-Gasteiz) 42(1), pp. 27-38. [Consulta 19 enero 2023]. ISSN 1578-1747.Disponible en:

https://www.sciencedirect.com/science/article/abs/pii/S0211139X07735850?via%3Dihub

12. RAMOS, P. & PINTO, J. "Health status of the elderly". Avances en Odontoestomatologia [en línea], 2015 (31), pp. 107-116. [Consulta: 19 enero 20231]. ISSN 0213-1285.Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213-12852015000300001&lng=es&nrm=iso&tlng=es.

13. VILLA, J., et al. "Adecuación de ingresos en el Servicio de Medicina Interna de un hospital de tercernivel". [en línea], 2019 [Consulta: 19 enero 2023].Disponible en: https://aprenderly.com/doc/3449257/adecuación-de-ingresos-en-el-servicio-de-medicina- interna.

14. WURGAFT, A. "Infecciones del tracto urinario". Revista Médica Clínica Las Condes [en línea], 2010, 21 (4), pp. 629-633. [Consulta: 24 febrero 2021]. ISSN 0716-8640. Disponible en: http://www.elsevier.es/es-revista-revista-medica-clinica-las-condes-202-articulo-infecciones-del-tracto-urinario-S0716864010705794.

15. MEDINA, M. & CASTILLO, E. "An introduction to the epidemiology and burden of urinary tract infections". Therapeutic Advances in Urology [en línea], 2019, 11 (3-7), pp.3-7 [Consulta: 19 enero 2023]. ISSN 1756- 2880. Disponible en: /pmc/articles/PMC6502976/.

16. INEC. Registro Estadístico de Camas y Egresos Hospitalarios 2019 [en línea]. Quito-Ecuador: Instituto Nacional de Estadística y Censos, 2019. [Consulta: 20 enero 2023]. Disponible en: www.ecuadorencifras.gob.ec.

17. ROJAS, P., et al. "Consumo de antimicrobianos en el Hospital Clínico-Quirúrgico Comandante Manuel Fajardo en el periodo 2016-2017". Revista 16 de abril [en línea], 2019 (58), pp. 9-14. [Consulta: 20 enero 2023]. ISSN 15308- 17241. Disponible en: http://www.rev16deabril.sld.cu/index.php/16_04/article/view/729.

18. MENÉNDEZ, R., et al. "Three keys to the appropriate choice of oral antibiotic treatment in the respiratory tract infections". Revista Española de Quimioterapia [en línea], 2019, (España) 32 (6), pp. 497- 515. [Consulta: 20 enero 2023]. ISSN 1988- 9518. Disponible en: /pmc/articles/PMC6913073/.

19. ALVO, A., et al. "Conceptos básicos para el uso racional de antibióticos en otorrinolaringología". Revista de otorrinolaringología y cirugía de cabeza y cuello [en línea], 2016, (Santiago), 76(1), pp. 136-147. [Consulta: 20 enero 2023]. ISSN 0718-4816. Disponible en: https://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0718-48162016000100019

20. PEÑAHERRERA, E. Uso De Antibacterianos En El Área De Clínica Del Hospital José Carrasco Arteaga". Facultad de Ciencias Químicas, Universidad de Cuenca [en línea], 2013 pp. 1-131. [Consulta: 20 enero 2023]. Disponible en: https://publicaciones.ucuenca.edu.ec/ojs/index.php/quimica/article/view/141/141.

21. MARTELL, N. & PRIETO, M. "Cuándo y por qué iniciar el tratamiento farmacológico con doble terapia". Semergen [en línea], 2012, 38(7), pp. 445-451. [Consulta: 25 enero 2023]. ISSN 1138-3593. Disponible en: http://www.elsevier.es/es-revista-medicina-familia-semergen-40-articulo-cuando-por-que-iniciar-el-S1138359312000974.

22. MARTÍNEZ, F., et al. "Monoterapia vs. terapia combinada en el tratamiento de las infecciones por bacterias gramnegativas multirresistentes". Revista Española de Quimioterapia [en línea], 2016 (España) 29 (1), pp. 43- 46. [Consulta: 25 enero 2023]. ISSN 0214- 3429. Disponible en: https://seq.es/wp-content/uploads/2015/02/seq_0214-3429_29_sup1_10sagasti.pdf.

23. KUTI, J. "Cómo Optimizar la Farmacodinamia Antimicrobiana: Una Guía para un Programa De Optimización del Uso De Antimicrobianos". Revista Médica Clínica Las Condes [en línea], 2016, (Estados Unidos) 27(5), pp. 625-635. [Consulta: 25 enero 2023]. ISSN 0716-8640. Disponible en: https://www.elsevier.es/es-revista-revista-medica-clinica-las-condes-202-articulo-como- optimizar-la-farmacodinamia-antimicrobiana-S0716864016300888

24. FLORES, J., et al. "Interacciones farmacológicas relacionadas con la administración de antibióticos betalactámicos". Revista de la Asociación Dental Mexicana [en línea], 2016, (México) 73(5), pp. 227-234. [Consulta: 25 enero 2023 Disponible en: https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=68471

25. CHAMORRO, M. "Cómo mejorar la prescripción antibiótica en la comunidad, ¿conocemos todas las claves?". Grupo de Patología Infecciosa de la Asociación Española de Pediatría de Atención Primaria [en línea], 2019, (España), pp. 1-17. [Consulta: 25 enero 2023]. Disponible en: https://www.aepap.org/sites/default/files/documento/archivos-adjuntos/doc_optimizacion_prescrip_atbs_ap_17-11-19.pdf.

26. MSP. Guías de práctica clínica. [en línea]. Quito- Ecuador: Ministerio de Salud Pública, 2017ª. [Consulta: 22 enero 2023]. Disponible en: https://www.salud.gob.ec/guias-de-practica-clinica/.

27. MSP. Ministerio de Salud Pública promueve el uso racional de medicamentos [en línea]. Quito- Ecuador, 2017b. [Consulta: 22 enero 2023]. Disponible en: https://www.salud.gob.ec/ministerio- de-salud-publica-promueve-el-uso-racional-de-medicamentos/.

28. MSP. Política Nacional de Medicamentos Aplicada en el Sistema de Salud. Quito- Ecuador: Ministerio de Salud Pública, 2017c [Consulta: 25 enero 2023]. Disponible en: www.msp.gob.ec.

29. MSP. Plan Nacional para la prevención y control para resistencia bacteriana. [en línea]. Quito-Ecuador, 2019 [Consulta: 25 enero 2023]. Disponible en: https://www.salud.gob.ec/wp-content/uploads/2019/10/Plan-Nacional-para-la-prevención-y-control-de-la-resistencia-antimicrobiana_2019_compressed.pdf.

30. BENEDÍ, J. & RAPOSO, C. "Antibioterapia en infecciones urinarias". Farmacia Profesional [en línea], 2005, (Madrid), 19(4), pp. 52-59. [Consulta: 25 enero 2023]. Disponible en: https://www.elsevier.es/es-revista-farmacia-profesional-3-articulo-antibioterapia-infecciones-urinarias-13074095.

31. ZBOROMYRSKA, Y., et al. Procedimiento de Microbiología Clínica. [en línea]. Madrid-España: Recomendaciones de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica, 2019. [Consulta: 25 enero 2023]. Disponible en: www.seimc.org.