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Antimicrobial Resistance in Genitourinary Infections: Mechanisms and New Therapeutic Strategies

Resistencia antimicrobiana en infecciones genitourinarias: mecanismos, y nuevas estrategias terapéuticas

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Abstract:

The rise of antibiotic-resistant infections is a critical public health issue, particularly due to the high prevalence of multidrug-resistant bacteria, which complicates treatment and places a significant burden on healthcare systems. This article aims to analyze the main mechanisms of antimicrobial resistance, such as the production of extended-spectrum β-lactamases, the activation of efflux pumps, and the modification of porins, which allow bacteria to evade the effects of antibiotics. In this context, urinary tract infections will be reviewed within the framework of resistance. Recent studies on antimicrobial resistance in bacteria causing genitourinary infections were collected, with a focus on current therapeutic strategies and emerging options. Existing strategies are discussed, highlighting the importance of rational antibiotic use, the implementation of rapid susceptibility testing, and the development of new alternatives, such as β-lactamase inhibitor combinations with β-lactam antibiotics and novel antimicrobials like plazomicin. Although these innovations offer new opportunities for treating resistant infections, preventing resistance requires control policies and epidemiological surveillance. In conclusion, to tackle antimicrobial resistance, it is crucial to implement responsible antibiotic use practices, strengthen rapid diagnostic strategies, and encourage research into innovative treatments.

Keywords:

Urinary tract infections (UTIs), Antimicrobial resistance, Extended-spectrum β-lactamases, Horizontal gene transfer, Multidrug-resistant bacteria

Resumen:

El aumento de infecciones resistentes a los antibióticos es un problema crítico en salud pública, especialmente debido a la alta prevalencia de bacterias multirresistentes, lo que complica su tratamiento y genera una carga considerable para los sistemas de salud. Este artículo tiene como objetivo analizar los principales mecanismos de resistencia antimicrobiana, como la producción de β-lactamasas de espectro extendido, la activación de bombas de eflujo y la modificación de porinas, que permiten a las bacterias evadir los efectos de los antibióticos. En este sentido, se revisarán las infecciones del tracto genitourinario dentro del contexto de resistencia. Se recopilaron estudios recientes sobre resistencia antimicrobiana por bacterias que causan las infecciones genitourinarias, con énfasis en las estrategias terapéuticas actuales y opciones emergentes. Se discuten las estrategias vigentes, destacando la importancia de un uso racional de los antibióticos, la implementación de pruebas de susceptibilidad rápida y el desarrollo de nuevas alternativas, como las combinaciones de inhibidores de β-lactamasa con antibióticos β-lactámicos y nuevos antimicrobianos como la plazomicina. Aunque estas innovaciones ofrecen nuevas oportunidades para tratar infecciones resistentes, la prevención de la resistencia requiere políticas de control y vigilancia epidemiológica. En conclusión, para enfrentar la resistencia antimicrobiana, es crucial implementar prácticas responsables en el uso de antibióticos, fortalecer las estrategias de diagnóstico rápido y fomentar la investigación en tratamientos innovadores.

Palabras Clave:

Infecciones genitourinarias (ITG), Resistencia antimicrobiana, β-lactamasas de espectro extendido, Transferencia genética horizontal, Bacterias multirresistentes

INTRODUCTION

Infectious diseases and their complications are a major cause of mortality, whose incidence decreased after the introduction of antimicrobial drugs in the 1940s, leading to an improved quality of life. Other public health measures that have contributed to better health status include water sanitation, immunizations, and the promotion of nutritious diets. The

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successful use of antibiotics has led to advances in medical-surgical techniques such as organ transplants, implant surgery, the care of premature newborns, and the treatment of immunocompromised patients, among others.[1]

Antimicrobial resistance (AMR) is an emerging problem that threatens the effectiveness of these drugs, as it complicates the treatment of many infections. Since the widespread introduction of antibiotics and their indiscriminate use as a treatment regimen, bacterial resistance mechanisms have also evolved, becoming a significant public health challenge.[2] AMR is the ability of certain microorganisms to survive and multiply even when exposed to high concentrations of antibiotics that would normally be lethal.[3] To measure this phenomenon, scientists use a parameter called the minimum inhibitory concentration (MIC), which indicates the minimum amount of antibiotic required to inhibit bacterial growth. However, some strains have developed the ability to withstand maximum concentration levels that would be lethal to other microorganisms of the same species. Bacteria can adapt, strengthen, and become difficult to eliminate through various mechanisms, such as: intrinsic resistance, in which structural characteristics make them naturally tolerant to certain antibiotics; genetic mutations that develop over time; or horizontal gene transfer, through which they acquire resistance genes from chromosomal fragments or plasmids.[4] As resistance mechanisms multiply and combine, the treatment of infections becomes more complex, highlighting the urgency of understanding how these processes are evolving.[2]

UTIs are among the most common infectious diseases worldwide, primarily affecting women, although they remain relatively under-researched.[5] In a study conducted among active-duty women in the Australian Defence Force, 41% of participants reported having experienced at least one UTI. UTIs and other genitourinary infections can impact the health and work performance of these women, emphasizing the importance of implementing prevention and management strategies within the military setting to reduce their impact.[6]

The most frequently isolated causative agent in UTIs is uropathogenic *Escherichia coli* (Fig. 1)[7], however, it is not the only species capable of colonizing the urinary tract (Fig. 2)[8]. The interaction between pathogenic microorganisms, the host's immune system, and the conditions present in the bladder determines the development and persistence of the infection.[5] A study conducted among university women who had experienced their first UTI episode revealed that 27% had at least one culture-confirmed recurrence within the following six months, and 2.7% experienced a second recurrence during the same period. When the initial causative agent is *Escherichia coli*, the likelihood of a new infection within the next six months is higher compared to other microorganisms. Another study involving women aged 17 to 82 with cystitis caused by *E. coli* showed that 44% experienced at least one recurrence within the following year.[9,10]

UTI AND ETIOPATHOGENESIS

The bacteria responsible for recurrent urinary tract infections (rUTIs) originate from the gut microbiota and use virulence factors, such as pili or fimbriae, to colonize the urinary tract. The characteristics of the vaginal and bladder epithelium also influence susceptibility to bacterial colonization, either facilitating or hindering the adherence of uropathogenic bacteria (Table 1).[11]

Table 1: *Adhesion Mechanisms and Virulence Factors in Recurrent Urinary Tract Infections (rUTIs).*

Epithelium	Adhesion Mechanism	Factor	Description
Vaginal Cells	Colonization Propensity	Receptors for *E. coli*	Women with rUTIs have a higher number of *E. coli* receptors in the vaginal epithelium.
		Genetic Factors	- HLA-A3 is associated with a higher risk of rUTIs. - Women over 65 years old have more uropathogens adhered to the vaginal epithelium.
		"Non-secretors" of ABO antigens	Women who do not secrete ABO antigens have a 3-4 times higher risk of rUTIs. Their epithelium facilitates uropathogen adhesion.
		Vaginal Fluid	In non-colonized women, vaginal fluid inhibits bacterial adhesion, with secretory immunoglobulin A (IgA)

			playing a key role.
Bladder Cells	Bacterial Adhesion	*E. coli* Type 1 Pili	*E. coli* type 1 pili bind to uroplakins in bladder cells, facilitating colonization.
	Bacterial Biofilms	Biofilm Formation	Bacteria form intracellular bacterial communities (IBC) similar to biofilms, allowing them to evade the immune response and persist in the urinary tract. This favors infection recurrence.
		Uromucoid (Tamm-Horsfall Protein)	Blocks adhesion of strains with type 1 pili. The absence of this protein increases *E. coli* colonization in animal models.

Note: Created based on the article "The global burden of antimicrobial resistance-urinary tract infections".[11]

The etiology of UTIs is based on identifying the microorganisms responsible for the infection, with their frequency varying according to age, sex, and the acquisition setting. In an analysis of 12,204 urine cultures, *Escherichia coli* was the most common pathogen, with a prevalence of 37–38% in adults and a higher incidence in children (59–64%). In adults, the next most frequent microorganisms were *Enterococcus faecalis* (16–18%) and *Klebsiella pneumoniae* (7–8%), while in children, *E. faecalis* reached 19% in community-acquired infections and 17% in hospital-acquired infections, followed by *Proteus mirabilis* (3–5%). Additionally, *Candida albicans* was the most prevalent fungus, with a frequency close to 5% in community infections and 4% in hospital infections. In terms of antibiotic susceptibility, no significant differences were found in the activity of antibiotics against *E. coli* in both adults and children, regardless of the infection acquisition setting. Similarly, *E. faecalis* and *P. mirabilis* in children showed no significant variations in antimicrobial susceptibility between community and hospital infections.[12]

In a study conducted with 457 children attending outpatient and emergency services at the Federico Gómez Children's Hospital in Mexico, presenting with symptoms of uncomplicated lower urinary tract infection, the causative pathogens were identified, and their antimicrobial susceptibility was evaluated. Urine samples were obtained by midstream clean-catch or catheterization. The most frequently isolated pathogens were *Escherichia coli* (68.3%), *Enterococcus spp*. (11%), *Klebsiella pneumoniae* (8.7%), *Pseudomonas aeruginosa* (7.5%), *Proteus mirabili*s (4.5%), and *Enterobacter cloacae* (1.7%).[13]

High resistance to various antibiotics was observed in some pathogens: resistance to trimethoprim/sulfamethoxazole was 73.7% in *E. coli*, 62.2% in *K. pneumoniae*, and 100% in *P. aeruginosa*, while resistance to ampicillin reached 86.3% in *E. coli* and 100% in *P. aeruginosa*. Regarding ciprofloxacin, resistance was lower, with only 33.8% of *E. coli* strains showing resistance. Nitrofurantoin, however, exhibited much lower resistance, especially among enterobacteria, with only 4.4% resistance in *E. coli*. These results highlight the high antimicrobial resistance in pathogens responsible for lower urinary tract infections in children, representing a significant challenge for the adequate treatment of these infections.[13]

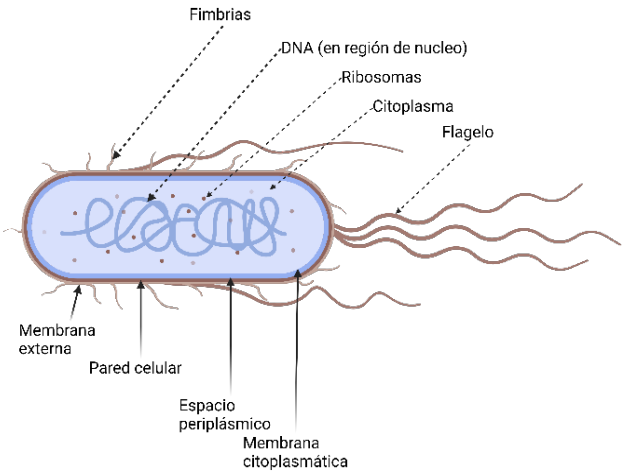

Figure 1. Structure of E. coli bacterium. Created by the author based on information about bacteria provided by the National Human Genome Research Institute (NHGRI).[7]

Risk factors for UTIS

The higher predisposition of women to UTIs is largely due to their anatomy (Fig. 2)[8], such as the short length of the urethra, which facilitates the entry of pathogens into the bladder.[14]

Additionally, behavioral, genetic, and urological factors also play important roles in the risk. Although it is known that some women are more prone to developing and maintaining recurrent UTIs, the reasons for this variability are not yet fully understood. It has been suggested that some Escherichia coli

strains, by forming extracellular and intracellular biofilms, may contribute to the persistence of infections by releasing bacteria in a delayed manner within the bladder.[14]

The risk factors for recurrent UTIs are similar to those for cystitis and are linked to the frequency of sexual intercourse, personal history of urinary infections, family history of UTIs in the mother, and having experienced the first episode before the age of 15. Other influences include the use of spermicides, recent antibiotic administration, and medical conditions such as diabetes. In postmenopausal women, urinary incontinence, the presence of cystocele, post-void residual urine, and a history of gynecological surgery increase susceptibility to these infections.[15]

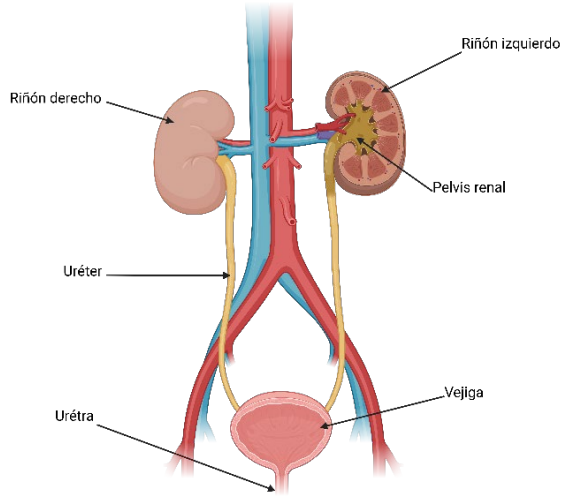

Figure 2. Anatomy of the urinary system. Created by the author based on the anatomy of the urinary system from the National Cancer Institute (NCI).[8]

Recurrent urinary tract infections (rUTIs) in women are a common condition that increases with age and usually occurs in patients without structural abnormalities of the urinary tract. Its origin is mainly due to vaginal colonization by uropathogens, facilitated by factors such as the use of spermicides, frequent sexual activity, maternal history of UTIs, and recent antimicrobial use. Despite its high prevalence, no association has been found between uncomplicated rUTIs and chronic kidney disease or hypertension. Prevention strategies include continuous or postcoital antimicrobial prophylaxis, the use of an oral vaccine, and estrogen replacement therapy in postmenopausal women. Additionally, treatments under development, such as vaginal vaccines and lactobacilli administration, have shown promising results.[15] However, other options like cranberry consumption or ascorbic acid have not demonstrated effectiveness in preventing recurrence. In selected cases, patient self-administered antimicrobial therapy has proven to be an effective alternative for women with good adherence to medical treatment.[16]

For the evaluation of women with rUTIs, a thorough medical history and physical examination are essential to identify possible risk factors and define specific studies. However, in most cases, recurrent infections are due to reinfections rather than anatomical or functional alterations of the urinary tract. Therefore, several studies question the usefulness of invasive procedures such as intravenous pyelography, voiding cystourethrography, and cystoscopy, as they often do not reveal abnormalities relevant to disease management. In the initial evaluation of patients without risk factors, non-invasive tests such as renal and pelvic ultrasound with measurement of post-void residual volume, as well as uroflowmetry, are prioritized. These studies allow the detection of alterations that would justify referral to a specialist.[11]

Recent research on the human urinary microbiome has enabled the development of specialized techniques to more precisely analyze a microbial community that is difficult to access and has low biomass**.** In the absence of UTIs, the concentration of microorganisms in urine is typically low, ranging from less than 100 to up to 10^5 colony-forming units (CFU) per milliliter.[17] This low microbial density requires particularly sensitive sampling and analysis methods, as highlighted by the study of Karstens et al.[18] Dysbiosis, understood as an imbalance in the microbial community, has been identified as a key factor in the predisposition to recurrent UTIs. The loss of protective commensal bacteria such as *Lactobacillus* and the increase of potentially pathogenic microorganisms like *Escherichia coli* promote colonization, perpetuate infection, and may contribute to the emergence of multidrug-resistant strains. This situation is exacerbated by the recurrent and non-specific use of antibiotics, which further disrupts the urinary ecosystem and perpetuates a vicious cycle of dysbiosis and infection.[18-20]

ANTIMICROBIAL TREATMENT

Antibiotic treatment of an acute episode of urinary tract infection (UTI) follows principles similar to the management of non-recurrent and uncomplicated UTIs. According to international guidelines, recommended first-line antibiotics include nitrofurantoin, fosfomycin trometamol, and pivmecillinam, while trimethoprim/sulfamethoxazole may be used in areas with *E. coli* resistance rates below 20%. Second-line options include cephalosporins. Treatment duration is usually short, generally between 1 and 5 days, depending on the antibiotic used. In mild cases without risk factors, a symptomatic management approach with increased fluid intake and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) can be considered to reduce the need for antibiotics and minimize resistance development.[15]

One study analyzed antimicrobial resistance in urinary tract infections in children over a five-year period. Resistance rates to various antibiotics were observed in bacteria isolated from urine samples of children with urinary infections. Among the key findings, a high prevalence of resistance to trimethoprim/sulfamethoxazole and ampicillin was found in

common pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. Additionally, resistance to last-line antibiotics such as ciprofloxacin and nitrofurantoin was notably low, suggesting that these options remain effective against some bacterial strains. This study underscores the importance of continuous monitoring of resistance rates to guide the treatment of urinary infections in children and highlights the growing concern about antimicrobial resistance in common pediatric infections.[21]

Goff et al. emphasize the urgent need for international and multidisciplinary collaboration to tackle antimicrobial resistance (AMR) by using antibiotics rationally through cooperation, mutual learning, and local adaptation. They also stress the importance of all healthcare professionals who prescribe antibiotics understanding the social impact of inappropriate use and adopting responsible practices. The publication provides concrete examples of how sharing experiences and effective policies can strengthen antimicrobial stewardship programs worldwide.[22]

ANTIMICROBIAL RESISTANCE IN UTIs

The pathogens most associated with antimicrobial resistance (AMR) in urinary tract infections (UTIs) are gram-negative bacteria. Uropathogens have developed both virulence and resistance mechanisms, indicating that these factors are often acquired together. The main resistance mechanisms studied in gram-negative bacteria include the production of extended-spectrum β-lactamases (ESBLs), which inactivate various β-lactam antibiotics; carbapenemases, capable of degrading carbapenems, considered last-line treatments; efflux pumps, which actively expel antibiotics from the bacterial cell; and porin modification, which reduces the entry of these drugs into the cell.[23] This resistance, especially in bacteria such as *Staphylococcus aureus* and *Escherichia coli*, has increased significantly over time, making eradication more complex and raising treatment costs.[24]

MECHANISMS OF ANTIMICROBIAL RESISTANCE

In a study conducted in 2024, antimicrobial resistance in urinary tract infections (UTIs) was addressed, focusing on pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterococcus*. The study analyzes various resistance mechanisms employed by these bacteria, including:

- Production of β-lactamases: Enzymes that inactivate β-lactam antibiotics.
- Modification of bacterial targets: Alterations in target proteins, such as penicillin-binding proteins and gyrases.
- Changes in membrane permeability: Modifications in porins that restrict antibiotic entry.
- Efflux pumps: Mechanisms that actively expel antibiotics from the bacterial cell.

Additionally, the article highlights the proliferation of *E. coli* strains that produce β-lactamase enzymes such as TEM and CTX-M, conferring resistance to first- and third-generation cephalosporins, as well as the rise of carbapenem-resistant strains—considered the last line of defense in severe infections. These findings underscore the urgent need to develop new therapeutic strategies to combat antibiotic-resistant UTIs.[11]

Among the main resistance mechanisms in gram-negative bacteria are the production of extended-spectrum β-lactamases (ESBLs), which inactivate various β-lactam antibiotics; carbapenemases, capable of degrading carbapenems—considered last-line treatments; efflux pumps, which actively remove antibiotics from the bacterial interior; and porin modifications, which reduce the entry of these drugs into the cell. These strategies enable bacteria to resist multiple treatments, complicating the management of UTIs and posing a significant challenge to healthcare systems worldwide.[23] A study analyzes the prevalence of antimicrobial resistance in Enterobacteriaceae isolated from the Peruvian Amazon region. The results reveal that a high percentage of Enterobacteriaceae strains are multidrug-resistant, with 57.4% of the isolates showing resistance to multiple antibiotics. Most of these strains produce extended-spectrum β-lactamases (ESBLs), with a notable prevalence of the *bla_CTX-M* gene. This situation highlights the growing concern over bacterial resistance in a region with limited medical resources, which complicates the treatment of severe infections. The study emphasizes the urgent need to implement effective control and prevention strategies to combat the spread of resistant strains, particularly in rural and hard-to-reach areas, where infections associated with these bacteria are more frequent.[25] Another study analyzes the prevalence of antimicrobial resistance in *Escherichia coli* isolated from clinical samples in hospitals in Peru, revealing growing concern over antibiotic resistance in the region. The results indicate that 57.4% of *E. coli* strains were multidrug-resistant, with a high prevalence of extended-spectrum β-lactamase (ESBL) producers, particularly the *bla_CTX-M* variants. This phenomenon highlights the urgent need for an appropriate control strategy against bacterial resistance, as therapeutic options are becoming significantly limited. The research also underscores the importance of epidemiological surveillance and the implementation of measures to prevent the spread of resistant strains in hospitals, especially in rural areas with limited medical resources.[26]

Antibiotic resistance represents one of the greatest challenges in modern medicine, as it has evolved rapidly since the first reports of penicillin resistance in the 1940s. Over time, the extensive and indiscriminate use of these drugs has driven the emergence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and, in the most critical cases, pan-resistant (PDR) bacteria—meaning that some infections no longer respond to any available treatment.[27] Resistance develops through specific mechanisms depending on the structure of the antibiotic and its mode of action, which may include inhibition

of cell wall synthesis, interference with DNA replication or protein synthesis, alteration of essential metabolic pathways, or disruption of the cytoplasmic membrane. However, bacteria have developed sophisticated strategies to counteract these effects, such as the production of enzymes that inactivate antibiotics, modification of their own cellular mechanisms to prevent drug action, active expulsion of antimicrobial compounds via efflux pumps, and the transfer of resistance genes between different bacterial species, which accelerates the spread of the problem. In addition to biological and genetic factors, the misuse of antibiotics in human and veterinary medicine, self-medication, lack of adequate infection control measures in hospitals, and the use of antimicrobials in agriculture have significantly contributed to the rise in resistance. This global health crisis not only complicates the treatment of common infections but also endangers essential medical procedures such as surgeries, organ transplants, and cancer treatments, which rely on the effectiveness of antibiotics to prevent secondary infections. In this context, it is crucial to develop strategies that include the responsible use of antibiotics, research into new antimicrobial therapies, and the implementation of epidemiological surveillance policies that enable more effective control of the spread of resistant bacteria.[28]

GENETIC TRANSFER MECHANISMS AND THEIR ROLE IN THE SPREAD OF ANTIBIOTIC RESISTANCE

Gene transfer plays a fundamental role in the spread of antimicrobial resistance (AMR), enabling bacteria to efficiently acquire and disseminate resistance genes. Among the genetic transfer mechanisms, horizontal gene transfer (HGT) is the primary pathway through which microorganisms exchange genetic information, facilitating rapid adaptation to hostile environments, such as those with high antibiotic pressure. The human gut microbiome functions as a vast reservoir of antibiotic resistance genes, allowing these genes to be transferred to opportunistic pathogens and contributing to the development of resistant infections. The irrational and prolonged use of antibiotics in clinical settings has increased the abundance of these genes in the gut, enhancing their transmission. Studies have shown that certain antibiotics, such as levofloxacin, can induce genetic transformation in bacteria like *Escherichia coli*, further promoting the spread of resistance. Multiple mechanisms regulate gene transfer, including the restriction-modification system, which acts as a bacterial defense against the entry of foreign DNA by degrading it before it can integrate into the genome. On the other hand, the CRISPR-Cas system, known for its role in bacterial adaptive immunity, limits the spread of mobile genetic elements such as plasmids and phages that may carry resistance genes. It has been observed that multidrug-resistant bacteria, such as certain enterococci, often lack CRISPR-Cas elements, suggesting that this system could act as a natural barrier against the dissemination of resistance genes. However, some phages have evolved anti-CRISPR proteins that inhibit this system, enabling gene transfer even in bacteria that possess CRISPR-Cas defenses. These gene transfer processes, driven by the selective pressure of excessive antibiotic use, have significantly contributed to the antimicrobial resistance crisis.[29]

NEW THERAPEUTIC STRATEGIES

Escherichia coli remains the primary etiological agent of community-acquired urinary tract infections (UTIs), showing high susceptibility to fosfomycin (96.5%) and nitrofurantoin (97.4%). However, resistance to commonly used antibiotics such as amoxicillin (58.1%), quinolones (36.6%), and trimethoprim-sulfamethoxazole (31.7%) limits their use in empirical treatment. These findings support the use of fosfomycin as a first-line treatment for uncomplicated cystitis in women under 65 years old and in men under 15 years old, while nitrofurantoin is a suitable option for women under 65 years old. Given the observed resistance pattern, empirical use of amoxicillin, amoxicillin-clavulanic acid, quinolones, and trimethoprim-sulfamethoxazole should be avoided in this clinical context.[30]

According to Bader et al., first-line antimicrobial agents such as trimethoprim-sulfamethoxazole, nitrofurantoin, and fosfomycin remain viable options for uncomplicated UTIs, but their efficacy has declined due to the emergence of resistant strains, particularly extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*.[31] In these cases, carbapenems, such as ertapenem, have been widely used as the treatment of choice for complicated infections or those caused by multidrug-resistant pathogens. However, the overuse of carbapenems has raised concerns about the spread of resistance to this class of antibiotics, prompting the search for new therapeutic alternatives. In response to this challenge, new combinations of β-lactamase inhibitors with β-lactam antibiotics have been developed, demonstrating high efficacy against resistant pathogens. Among them, ceftolozane-tazobactam and ceftazidime-avibactam have shown significant activity against resistant Enterobacteriaceae, including ESBL-producing strains and some carbapenem-resistant isolates. Another promising agent is meropenem-vaborbactam, which combines a carbapenem with a potent β-lactamase inhibitor, providing coverage against carbapenem-resistant bacteria mediated by the KPC enzyme (*Klebsiella pneumoniae* carbapenemase). In addition to these combinations, new antibiotics with innovative mechanisms of action have been developed. Plazomicin, a next-generation aminoglycoside, has demonstrated efficacy against resistant Enterobacteriaceae, including those with aminoglycoside-modifying enzyme-mediated resistance. This agent is considered a viable option for treating complicated UTIs caused by multidrug-resistant organisms. Similarly, imipenem-relebactam has emerged as a promising therapeutic alternative for infections caused by multidrug-resistant pathogens by combining a carbapenem with a potent β-lactamase inhibitor.

To improve treatment effectiveness and reduce the emergence of resistance, the importance of rapid susceptibility testing and personalized antimicrobial therapy has been emphasized. The implementation of molecular diagnostic tools allows for more precise identification of resistance mechanisms present in pathogens, facilitating the selection of the most appropriate antibiotic and minimizing unnecessary use of broad-spectrum antimicrobials. Additionally, strategies such as antibiotic de-escalation and monitoring antibiotic blood levels have proven effective in optimizing UTI treatment.[31]

Advances in bacterial culture and DNA sequencing techniques have allowed the identification of a more diverse and previously unrecognized urinary tract microbiome (urobiome). This microbiome may play a crucial role in health and disease, particularly in urinary tract infections (UTIs), giving it significant clinical relevance. Although various studies have confirmed the existence of a core urobiome, the role of the microbes that compose it is not yet fully understood, especially in relation to health and disease. In this article, we review the current state of research and conclude that the urobiome is an essential component of the body's innate immune defenses and a valuable resource for developing new strategies for the treatment and control of UTIs.[18-20]

CONCLUSION

Genitourinary infections represent a global public health problem due to their high prevalence and the increasing antimicrobial resistance. The overuse of antibiotics has favored the emergence of multidrug-resistant bacteria, complicating treatment and leading to higher therapeutic failures, hospitalizations, and costs. Among the resistance mechanisms, the production of extended-spectrum β-lactamases (ESBL) and horizontal gene transfer stand out. In this context, it is essential to promote the rational use of antibiotics, implement rapid susceptibility testing for timely diagnosis, and develop new therapeutic strategies and global surveillance policies to contain the spread of resistance genes in clinical and community settings.

REFERENCES

[1] Peebles K, Velloza J, Balkus JE, McClelland RS, Barnabas RV. High global burden and costs of bacterial vaginosis: a systematic review and meta-analysis. Sex. Transm. Dis. 2019; 46(5): 304-11.

[2] Alós JI. Resistencia bacteriana a los antibióticos: una crisis global. Enferm. Infecc. Microbiol. Clin. 2015; 33(10): 692-9.

[3] Brauner A, Fridman O, Gefen O, Balaban NQ. Distinguishing between resistance, tolerance and persistence to antibiotic treatment. Nat. Rev. Microbiol. 2016; 14(5): 320-30.

[4] Huemer M, Mairpady Shambat S, Brugger SD, Zinkernagel AS. Antibiotic resistance and persistence-implications for human health and treatment perspectives. EMBO Rep. 2020; 21(12): e51034.

[5] Murray BO, Flores C, Williams C, Flusberg DA, Marr EE, Kwiatkowska KM, et al. Recurrent urinary tract infection: A mystery in search of better model systems. Front. Cell. Infect. Microbiol. 2021; 11: 691210.

[6] O'Shea SD, Pope R, Freire K, Orr R, Gallagher N. Genitourinary infections in Australian servicewomen. Neurourol. Urodyn. 2023; 42(8): 1668-75.

[7] National Human Genome Research Institute. Bacteria [Internet]. 2024 [cited 2025 Feb 17]. Available from: https://www.genome.gov/es/genetics-glossary/Bacteria

[8] Instituto Nacional del Cáncer. Infección urinaria [Internet]. Diccionario de cáncer. 2024 [cited 2025 Feb 17]. Available from: https://www.cancer.gov/espanol/publicaciones/diccionarios/diccionario-cancer/def/infeccion-urinaria

[9] Alós JI. Epidemiología y etiología de la infección urinaria comunitaria. Sensibilidad antimicrobiana de los principales patógenos y significado clínico de la resistencia. Enferm. Infecc. Microbiol. Clin. 2005; 23 (Suppl 1): 3-8.

[10] Ikäheimo R, Siitonen A, Heiskanen T, Kärkkäinen U, Kuosmanen P, Lipponen P, et al. Recurrence of urinary tract infection in a primary care setting: analysis of a 1-year follow-up of 179 women. Clin. Infect. Dis. 1996 Jan; 22(1): 91-9.

[11] Von Vietinghoff S, Shevchuk O, Dobrindt U, Engel DR, Jorch SK, Kurts C, et al. The global burden of antimicrobial resistance–urinary tract infections. Nephrol. Dial. Transplant. 2024; 39(4): 581-8.

[12] Artero-López J, Gutiérrez-Soto B, Expósito-Ruiz M, Sorlózano-Puerto A, Navarro-Marí JM, Gutiérrez-Fernández J. Etiología de las infecciones urinarias en nuestra área sanitaria y perfil de sensibilidad de los uropatógenos más frecuentes. Arch. Esp. Urol. 2021; 74(2): 97-207.

[13] López-Martínez B, Calderón-Jaimes E, Olivar-López V, Parra-Ortega I, Alcázar-López V, Castellanos-Cruz MDC, et al. Susceptibilidad antimicrobiana de microorganismos causantes de infección de vías urinarias bajas en un hospital pediátrico. Bol. Med. Hosp. Infant. Mex. 2014; 71(6): 339-45.

[14] Zare M, Vehreschild MJGT, Wagenlehner F. Management of uncomplicated recurrent urinary tract infections. BJU Int. 2022; 129(6): 668-78.

[15] Valdevenito SJP. Infección urinaria recurrente en la mujer. Rev. Chilena Infectol. 2008; 25(4): 268-76.

[16] Valdevenito JP, Álvarez D. Infección urinaria recurrente en la mujer. Rev. Méd. Clínica Las Condes. 2018; 29(2): 222-31.

[17] Rowe TA, Juthani-Mehta M. Urinary tract infection in older adults. Aging Health. 2013; 9(5): 10.2217/ahe.13.38.

[18] Karstens L, Asquith M, Caruso V, Rosenbaum JT, Fair DA, Braun J, et al. Community profiling of the urinary microbiota: considerations for low-biomass samples. Nat. Rev. Urol. 2018; 15(12): 735-49.

[19] Neugent ML, Hulyalkar NV, Nguyen VH, Zimmern PE, De Nisco NJ. Advances in understanding the human urinary microbiome and its potential role in urinary tract infection. mBio. 2020; 11(2): e00218-20.

[20] Jones J, Murphy CP, Sleator RD, Culligan EP. The urobiome, urinary tract infections, and the need for alternative therapeutics. Microb. Pathog. 2021; 161(Pt B): 105295.

[21] Moriyama B, Henning SA, Neuhauser MM, Danner RL, Walsh TJ. Continuous-infusion beta-lactam antibiotics during continuous

venovenous hemofiltration for the treatment of resistant gram-negative bacteria. Ann. Pharmacother. 2009; 43(7): 1324-37.

[22] Goff D, Kullar R, Goldstein E, Gilchrist M, Nathwani D, Cheng A, et al. A global call from five countries to collaborate in antibiotic stewardship: united we succeed, divided we might fail. Lancet Infect. Dis. 2017; 17(2): E56-63.

[23] Lepe JA, Martínez-Martínez L. Puesta al día en Medicina Intensiva: infecciones graves por gramnegativos multirresistentes. Mecanismos de resistencia en bacterias gramnegativas. Medicina Intensiva. 2022; 46(7): 392-402.

[24] Castro-Orozco R, Barreto-Maya AC, Guzmán-Álvarez H, Ortega-Quiroz RJ, Benítez-Peña L. Patrones de resistencia antimicrobiana en uropatógenos gramnegativos aislados de pacientes ambulatorios y hospitalizados Cartagena, 2005-2008. Rev. Salud Pública (Bogotá). 2010; 12(6): 1010-9.

[25] León-Luna D, Fajardo-Loyola A, Yareta-Yareta J, Burgos-Espejo A, Peralta-Siesquen C, Galarza-Pérez M, et al. Caracterización molecular de enterobacterias multirresistentes en dos departamentos de la selva peruana. Biomédica. 2021; 41(Sp. 2): 180-7.

[26] Guzmán M, Salazar E, Cordero V, Castro A, Villanueva A, Rodulfo H, et al. Multirresistencia a medicamentos y factores de riesgo asociados con infecciones urinarias por Escherichia coli adquiridas en la comunidad, Venezuela. Biomedica. 2019; 39(s1): 96-107.

[27] Džidić S, Šušković J, Kos B. Antibiotic resistance mechanisms in bacteria: Biochemical and genetic aspects. Food Technol. Biotechnol. 2008; 46(1): 11-21.

[28] Pulingam T, Parumasivam T, Mohd Gazzali A, Mohd Sulaiman A, Chee JY, Lakshmanan M, et al. Antimicrobial resistance: Prevalence, economic burden, mechanisms of resistance and strategies to overcome. Eur. J. Pharm. Sci. 2021; 170: 106103.

[29] Tao S, Chen H, Li N, Wang T, Liang W. The spread of antibiotic resistance genes in vivo model. Can. J. Infect. Dis. Med. Microbiol. 2022; 2022(1): 3348695.

[30] Aguinaga A, Gil-Setas A, Mazón Ramos A, Alvaro A, García-Irure JJ, Navascués A, et al. Infecciones del tracto urinario. Estudio de sensibilidad antimicrobiana en Navarra. An. Sist. Sanit. Navar. 2018; 41(1): 17-26.

[31] Bader MS, Loeb M, Leto D, Brooks AA. Treatment of urinary tract infections in the era of antimicrobial resistance and new antimicrobial agents. Postgrad. Med. 2020; 132(3): 234-50.