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Literature on Antibiotic Resistance in Urinary Tract Infections in Case of Pregnancy and HIV

Kambale Kisuba[1,2*]; Paluku Maghulu[1]; Kakule Mbaghendyabo[1,2]

[1]Higher Institute for Medical Techniques of Goma (ISTM-GOMA, Democratic Republic of the Congo
[2]Medilab Center, Democratic Republic of the Congo

Corresponding Author: Kambale Kisuba[*]

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Abstract: Urinary tract infection (UTI) among pregnant women can lead to adverse maternal and fetal outcomes. Human Immunodeficiency Virus (HIV) results in increased likelihood of opportunistic infections, including UTI. Antimicrobial resistance may contribute to persistence of UTI and, this may differ accordingly to age of the pregnancy, types of UTI and HIV clinical stages. Anatomical and physiological characteristics make UTIs particularly prevalent among women, especially those who are pregnant. These infections, whether they exhibit symptoms or not, pose significant risks to expecting mothers and their offspring. Furthermore, the risk of a UTI returning post-treatment adds a layer of complexity to its care. While there is a wide array of antimicrobial drugs availablefor treating infections, it is a matter of concern that antimicrobial resistance rapidly emerges followingthe approval of new drugs for clinical use. These, directly concerns the World Health Organization (WHO) to initiate a Global Action Plan in order to correctly address the problem of antimicrobial resistance in 2015. The current literature highlights the main bacteria found in UTIs, various family of antibiotic used in case of UTIs, reasons behind antibiotic resistance and the mechanisms of bacterial resistance. Approximately 8% of women with pregnancy experience infections of their urine system, and if left untreated, these infections may lead towards severe consequences like pyelonephritis, lower birth weight, pretermlabor, as well as sepsis. It is significant noting that the use of sulfonamides and nitrofurantoin during pregnancy carries potential risks of birth defects, counting heart defects, anencephaly, as well as orofacial clefts. Amongst the bacteria'sspecies *E. coli* accounts to 80% up to 85% of the infections; the *Staphylococcus* spp that institutes to 10% up to 15%. Additionally, bacterial species *Klebsiella, Proteus, Pseudomonas*, aswell as *Enterococcus* spp plays slight function in deliberating the bacterial illness in urinary tract. Human immunodeficiency virus (HIV) and pregnancy significantly increase the susceptibility for opportunistic bacteria, urinary tract infections (UTIs) being part of them. This is especially problematic in developing nations whereby access to adequate healthcare services remains limited. Numerous studies have demonstrated an important rate of the bacteriuria without symptoms among female HIV- positive compared to HIV- negative pregnant women. In this vulnerable population of HIV-infected pregnant women, the normal use of the trimethoprim - sulfamethoxazole prevention might potentially elevate the risks of developing Multi-Drug-Resistant (MDR) bacterial diseases. Urinary tract infections, typicallycaused by bacteria, can progress to more severe conditions, like blood infections and pyelonephritis, particularly in individuals with underlying risk factors. This may lead to hospitalization of HIV-infected patients. Exposure to antimicrobials can lead to an increased prevalence of bacteria found to be drug-resistant in both animals and humans being, which, in turn, can lead to extension of hospital stays and higher rates of illness and death in the human population. For the urinary tract infections treatment in case of pregnancy, Cephalexin or Nitrofurantoin are commonly prescribed since they are mostly considered safe for pregnant women. This require laboratory screening for prescription guidance.

Keywords: *Literature, Antibiotic Resistance, UTI, Pregnancy, HIV.*

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I. INTRODUCTION

Urinary tract infections (UTIs) commonly occur when bacteria, coming from the skin or rectum, penetrate the urethra and contaminate the urinary system. Such infections can target several areas of the urinary system. Bladder infections, known as cystitis, are the most prevalent kind, while kidney infections, termed pyelonephritis, are rarer but carry more severe implications [1].

A UTI impacting the lower urinary tract is termed cystitis, whereas one affecting the upper urinary tract is

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labeled pyelonephritis. HIV-infected individuals, people living with diabetes, pregnant women, etc. have heightened susceptibility to UTIs, largely attributed to their compromised immune system. Thus, in case of antibiotic abuse and bad prescription, bacterial resistance can occur [2].

Urinary Tract Infections are caused by wider range of microorganisms, counting Gram Negative as well as Gram Positive Bacteria, and Fungi. Besides, none-complicated UTIs, naturally, affect women, younger as well as elderly people whom are otherwise healthy. The complicated UTIs are in general related to indwelling catheters, immunosuppression, urinary system abnormalities or exposure towards antibacterial medicines. Thus, the most common contributing agent for uncomplicated as well as complicated urinary system infections remains uro-pathogenic *Escherichia coli* (UPEC). The uncomplicated urinary system infections, other causative microorganisms are (in orders of prevalence) *Klebsiella pneumoniae, Staphylococcus saprophyticus, Enterococcus faecalis*, group B *Streptococcus* (GBS), *Proteus mirabilis, Pseudomonas aeruginosa*,*Staphylococcus aureus* and *Candida spp.* On the other hand, complicated urinary system infections, other causative microorganisms also are (in orders of prevalence) *Enterococcus spp., K. pneumoniae, Candida* spp., *S. aureus, P. mirabilis, P. aeruginosa* as well as GBS [3].

II. ANTIMICROBIAL AGENTS AGAINST UTIS

- *Trimethoprim-Sulfamethoxazole*

Trimethoprim-sulfamethoxazole also is widely accepted as the go-to cure for both initial and persistent urinary-system bacterial problems due to its effectiveness against the well-known uro – pathogens, cost-effectiveness, and to be tolerated. This combination of trimethoprim and sulfamethoxazole has a synergistic action, impacting two separate stages of bacterial folate metabolism, ultimately hindering DNA synthesis [4].

For individuals with a sulfa allergy, trimethoprim alone can be a suitable alternative, as studies have demonstrated a comparable cure rate to trimethoprim-sulfamethoxazole. Common adverse effects, affecting approximately 3% up to 5% of the patients, include skin rashes, nausea, as well as to vomit. Greater side effects, like anemia and the syndrome of Stevens-Johnson, are less frequent but necessitate vigilant monitoring. Patients with glucose-6-phosphate dehydrogenase deficiency, as well as those with renal and hepatic impairments, should use trimethoprim-sulfamethoxazole cautiously. Notably, the use of trimethoprim-sulfamethoxazole can potentially intensify the glucose-lowering effect of sulfonylureas like glipizide. Additionally, when administered alongside sodium warfarin, this medication may elevate the risk of bleeding, necessitating close monitoring [4].

- *Fluoroquinolones*

Fluoroquinolones are the class of broad-spectrum antibiotics known for their ability to inhibit enzymes like topoisomerase II (DNA gyrase) and topoisomerase IV. These drugs exhibit varying degrees of effectiveness against different types of bacteria, but they generally perform well against Gram-negative uropathogens, various *S. saprophyticus* and Enterobacteriaceae. Levofloxacin and Ciprofloxacin are the two frequently prescribed fluoroquinolones for treating urinary tract infection, and they tend to cause minimal sides effects like nausea, dizziness, diarrhea, photosensitivity, as well as headache [4].

One important consideration when using fluoroquinolones is their interaction with products containing cations like magnesium, calcium, iron, multivitamins, aluminum, or zinc, with minerals. These substances can significantly reduce the absorptions of the fluoroquinolones from gastro-intestinal systems. Patients should effectively take these antibiotics either 2 hours before or 4 hours after consuming products having cations components. Additionally, it's worth noting that levofloxacin and ciprofloxacin can affect the metabolism of theophylline and caffeine. Therefore, caution is needed when these drugs are used alongside these compounds. It's also crucial to monitor patients closely when warfarin, an anticoagulant, is coadministered with a fluoroquinolone. This combination can potentially lead to increased anticoagulation. Importantly, fluoroquinolones should not be used by pregnant or breastfeeding women due to safety concerns [4].

However, not all fluoroquinolones are suitable for treating urinary tract infections because of their varying pharmacokinetic profiles. Moxifloxacin and Sparfloxacin, for instance, achieve low concentrations within the urine compared to other quinolones as well as are not accepted for this particular indication. Gatifloxacin and moxifloxacin, which fall under the category of 8- methoxyquinolones, offer an extended spectrum of action, including improved effectiveness against anaerobic plus Gram-positive bacterial. Nonetheless, they do not offer any advantages in the treatments of the Urinary Tract Infections [4].

- *B-Lactam*

Previously, Urinary Tract Infections (UTIs) were commonly cured using β-lactam molecules like first-generation cephalosporins (e.g., cephalexin) as well as aminopenicillins (e.g., ampicillin and amoxicillin). These drugs were favored due to their capacity to achieve high level of concentration in the urinary tract. However, due to increasing resistance and high recurrence ratios compared to other treatment options, these antibiotics are not recommended as the first-lines therapy for UTIs. Instead, their use should be restricted to cases where a urine culture confirms their effectiveness [4].

Third-generation cephalosporins, like cefixime and the cefpodoxime, offer several advantages. They have longer half-lives, which means less frequent dosing is required. Additionally, these antibiotics have shown lower resistance rates against *E. coli* when compared to first-generation cephalosporins and aminopenicillins. Therefore, they can be considered as alternatives for patients who cannot tolerate trimethoprim-sulfamethoxazole or when dealing with

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resistant infections. Common side impacts of β-lactam antibiotics include skin rashes, nausea, abdominal discomfort, vomiting, and headaches. These drugs work by inhibiting bacterial cell wall synthesis. It is crucial to note that individuals with a history of severe β-lactam allergies, such as anaphylactic reactions or hives, should avoid using cephalosporins and penicillins [4].

➢ *Nitrofurantoin*

Nitrofurantoin is offered in two different forms: Monohydrate-macrocrystal (Macrobid) and macrocrystalline (Macrodantin). It operates by inhibiting various bacterial metabolic enzyme – systems and potentially impacting cell walls synthesis. Besides, Macrodantin necessitates a dosing schedule every six hours, while Macrobid only requires two daily doses. Approximately 90% of nitrofurantoin is excreted through the kidneys, mainly through glomerular filtration as well as tubular secretion. When a patient's projected creatinine clearance falls below 0.83 mL per second (less than 50 mL per minute), the drug is not effective in achieving sufficient antibacterial concentrations in the urine and should not be administered. The drug's side impacts are typically mild and might include symptoms like cough, malaise, and shortness of breath. Instances of pulmonary fibrosis are infrequent, and they are typically associated with treatment lasting longer than half a year [4].

➢ *Fosfomycin Tromethamine*

Fosfomycin, a derivative of phosphoric acid, remains primarily prescribed to address straightforward urinary tract infection. Besides, it is mainly administered in a single 3-gram oral dose. Besides, Fosfomycin operates by inhibiting pyruvyl transferases, an enzyme crucial for initiating bacterial cell wall synthesis. Its effectiveness encompasses a range of bacteria, such as *E. coli*, Enterococci, Citrobacter, Serratia, Enterobacter, as well as *Klebsiella spp.* However, it does not extend to *S. saprophyticcus.* Fosfomycin remains accessible as the powder and mixed effectively with 3 to 4 ounces of clean-water for oral consumption. Generally, it is also easily-taken, though some individuals may experience side effects such as diarrhea (9%), alongside occasional instances of nausea, vomiting, and esophageal discomfort [4].

III. SUMMARY

In the treatments scales for the simple urinary tract infections in female, the primary choice is typically trimethoprim-sulfamethoxazole or trimethoprim due to their affordability and effectiveness. These antibiotics should be the first-line therapy unless the community's uropathogens exhibit a resistance rate exceeding 10% to 20%. In such cases, alternative options may be considered. Fluoroquinolones, which are more expensive and have a broader spectrum, should be set aside for the communities with high resistance rates to the trimethoprim (higher than 10% up to 20%) or for sufferer-persons whom cannot stand trimethoprim-sulfamethoxazole or experience frequent UTIs. Besides, different treatment choices are the 7-day course of nitrofurantoin or the single dosage of fosfomycin [4].

It is advisable to avoid the use of first-generation aminopenicillins or cephalosporins due to their high degrees of resistance and increased risk of recurrence. While insensitivity to 3rd-generation Cephalosporins is generally lower concentration than that of 1st-generation Cephalosporins, these antibiotics are considered the 3rd-line options due to limited affordability and comparable effects [4].

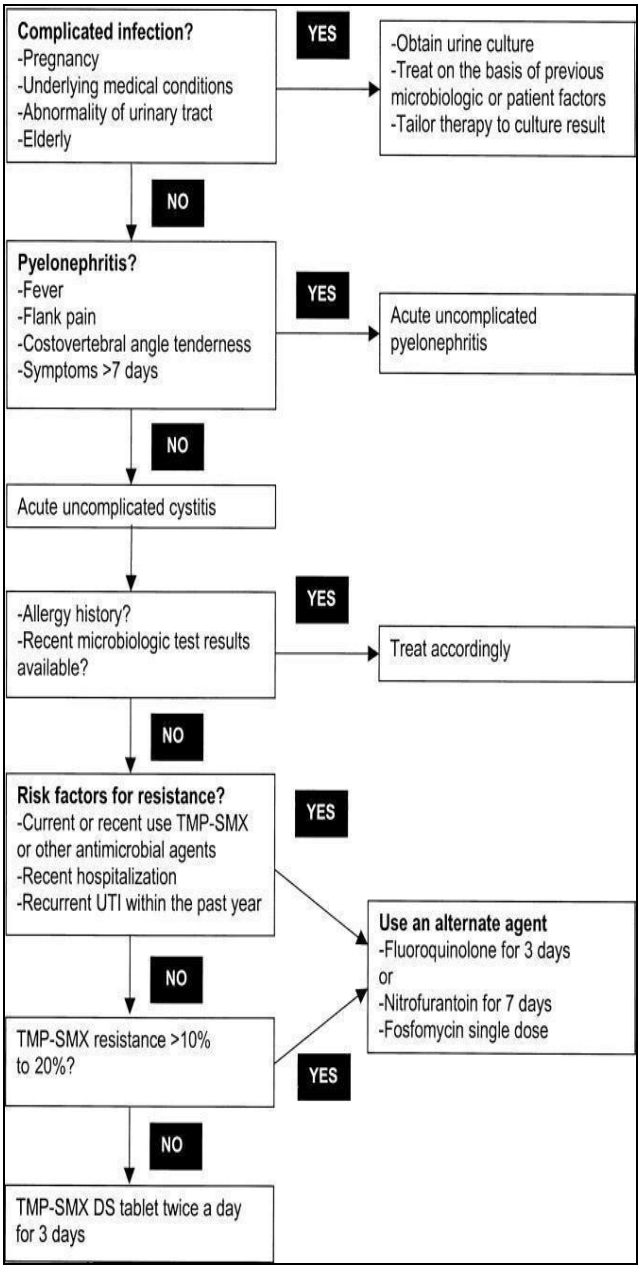

Fig 1 Outline of the Treatment of Uncomplicated Urinary Tract Infections in Women [5].

➢ *Urinary Tract Bacterial Resistance to Antibiotics*

Clinicians should be vigilant in understanding the resistance patterns of uropathogens in their communities, particularly when treating uncomplicated urinary tract infections empirically. Recent data indicates a significant impact of resistant uropathogens on empirical therapy, with the most notable rise in resistance being observed for trimethoprim-sulfamethoxazole. For example, a study

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curried out in the Seattle area found that *E. coli* resistances towards trimethoprim and the trimethoprim-sulfamethoxazole improved from 9% in 1992 to 18% in 1996 among outpatient women aged 18 to 50 with acute cystitis [4].

Additionally, the same study revealed substantial resistance in *E. coli* to β-lactams like ampicillin (34%) and First-Generation cephalosporins (28%). To gain a broader perspective on regional resistance patterns, a national survey in 1998 examined urine isolates from female outpatients. Notably, the west of United States, including Oregon, Washington, and California had the highest *E.coli* resistance (22%), while the Northeast displayed the lowest resistance (10%). Thus, *E. coli* resistance towards nitrofurantoin and fluoroquinolones remains relatively low. Besides, the Infectious disease society of America has recently revised guidelines for antibacterial treatment inuncomplicated acute bacteria cystitis as well as pyelonephritis among women. They recommend the use of trimethoprim or the trimethoprim-sulfamethoxazole as the first-line empirical therapy only within populations where uropathogen non-sensitive towards trimethoprim remains less than 10% to 20% [4].

➢ *Reasons Behind Antibiotic Resistance*

Bacteria and other microorganisms continuously evolve to ensure their survival, reproduction, and expansion. These adaptive behaviors make them proficient at overcoming challenges in their environment, such as the presence of antibiotics. When confronted with these drugs, bacteria might undergo genetic changes, allowing them to become resistant and continue thriving [6]. This inherent ability of bacteria to develop resistance is influenced by multiple factors. These factors include excessive use of antibiotics, poor diagnosis leading to incorrect antibiotic prescription, the decrease in patient sensitivity, self-medication habits, inadequate healthcare infrastructure, lack of personal hygiene, as well as the prevalent usage of the antibiotics within agriculture [7, 8, 9].

IV. MICROBIAL (NATURAL) REASONS

➢ *Generic Mutation*

During bacterial replication, small changes can occur in a few base pairs, known as point mutations. These mutations have the potential to replace specific amino acids critical for various functions, including enzymes, cell walls, and cellular structures. Additionally, they can impact regulatory genes and the overall structure of the chromosome. This adaptation can lead to the rise of new bacterial straining with the resistance to antibiotics. These newly acquired defense mechanisms can render previously effective antibiotics ineffective. This means that antibiotics, which were originally designed to combat these bacteria for extended periods, may no longer be as effective as they once were [10].

➢ *Genetic Material Transfer*

Resistance to antibiotics can be acquired by previously susceptible strains of bacteria. Many of the genes that are involved for antibacterial resistances are found on mobile genetic elements, including plasmids. These genetic elements have the potential to transfer between bacteria of various genera and species. Besides, bacteria with drug-resistant capacity have the ability to transfer copies of their resistance genome towards other existing bacteria known to be non-resistant. As a result, these bacteria without any resistance can acquire the newer genetic material and, over time, create drug resistance [10].

➢ *Selective Pressure*

This pressure can be well-defined as a set of environmental circumstances that create a favorable environment for the survival as well as propagation of the organisms with unique mutations or recently acquired traits. When microbes are exposed to antimicrobial agents, they can either be eliminated or, if they possess resistance genes, they will endure the treatment. As a result, those resilient microbes will multiply and gradually become the dominant form within the microbial population, outcompeting non-resistant counterparts [11, 12, 13].

➢ *Inaccurate Diagnosis*

In the process of diagnosing infections, healthcare practitioners occasionally resort to uncertain or imprecise information, leading to instances where they prescribe antibiotics "just in case" or opt for broad-spectrum antibiotics when a more specific, narrow-spectrum option may be much suitable. This kind of situation contributes significantly to the acceleration of antimicrobial resistance [9, 14].

➢ *Unsuitable Prescription of the Antibiotic*

In situations where medical professionals are uncertain whether an infection remains primarily caused by bacteria or the virus, they might opt to prescribe antibiotics. It is significant to note that the antibiotics are futile against viral infections and can potentially lead towards the developments of antibiotic resistance [15, 16].

➢ *Self-Medication*

The Southeast Asian region witnesses a common practice of using antibiotics without the guidance of a physician, referred to as self-medication with antibiotics (SMA) (Nepal & Bhatta, 2018). This behavior is associated with the potential for inappropriate usage of drugs, jeopardizing patient safety by increasing the drug adverse reactions risk, concealing the signs of underlying health conditions, and facilitating microbes to become resistant towards a number of molecules [17].

➢ *Insufficient as Well as Overuse of the Antibiotics*

Failing to complete a full course of antibacterial molecules can lead to certain bacteria thriving and developing resistance to the specific antibiotic. As far back as 1945, Alexander Fleming, the pioneer of antibiotics, cautioned the public about the risks linked to the improper consumption of these medications. Overusing antibiotics or taking them for inappropriate reasons can introduce genetic changes in bacteria, rendering the antibiotics ineffective against them [17].

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➢ *Lack of Hygiene*

Every day, hospitals receive a multitude of individuals, including patients, staff, and visitors, each carrying a unique array of microbiomes and colonizing bacteria on their clothing as well as within their bodies. Without proper procedures and the protocols in place in order to ensure cleanliness, these bacteria can proliferate and facilitate the emergence as well as dissemination of the antimicrobial resistance (AMR) [17].

➢ *Extensive Usage in Agriculture*

Antibiotics are commonly used as the growth supplements as well as promoter for animals in both industrialized and emerging regions globally. Similar to their use in humans, administering antibiotics to livestock leads to the emergence of bacteria with antibiotic-resistance capacity. These antibiotic- resistant bacteria, when found in livestock, can provoke a threat to health in human-being as they have the potential to be pathogenic to humans. Furthermore, these bacteria may use the food-chain transmission within humans as well as are widely disseminated within the environment via animal waste. This transmission and environmental circulation can result in the development of untreatable, complex, and long-term infections in humans [7].

➢ *Availability of New Antibiotics*

Pharmaceutical industry has faced significant challenges in developing new antibiotics to combat antibiotic- resistant bacteria. These challenges include technical difficulties, limited knowledge, complexities associated with bacterial activities (like the intricate Gram-negative cell walls), and various economical and governing obstacles. Unfortunately, whenever new antibiotics are introduced, the rapid development of antibiotic resistance is almost inevitable [7]. Consequently, doctors tend to reserve these novel medications for most severe cases, whereas enduring to effectively administer older, frequently generic medicines that have revealed comparable effectiveness. This practice raises concerns about the potential development of resistance in bacteriatowards these older antibiotics [15].

V. MECHANISM OF ACTION OF ANTIBIOTICS

The action pathways of antibiotics are typically categorized into five primary modes. These include interference with the synthesis of cell wall for the bacterial structure, blocking the production of bacterial parotids, halting the combination of the bacterial genetic material, impeding metabolic pathways, and disrupting the activity of the bacterial membrane [18].

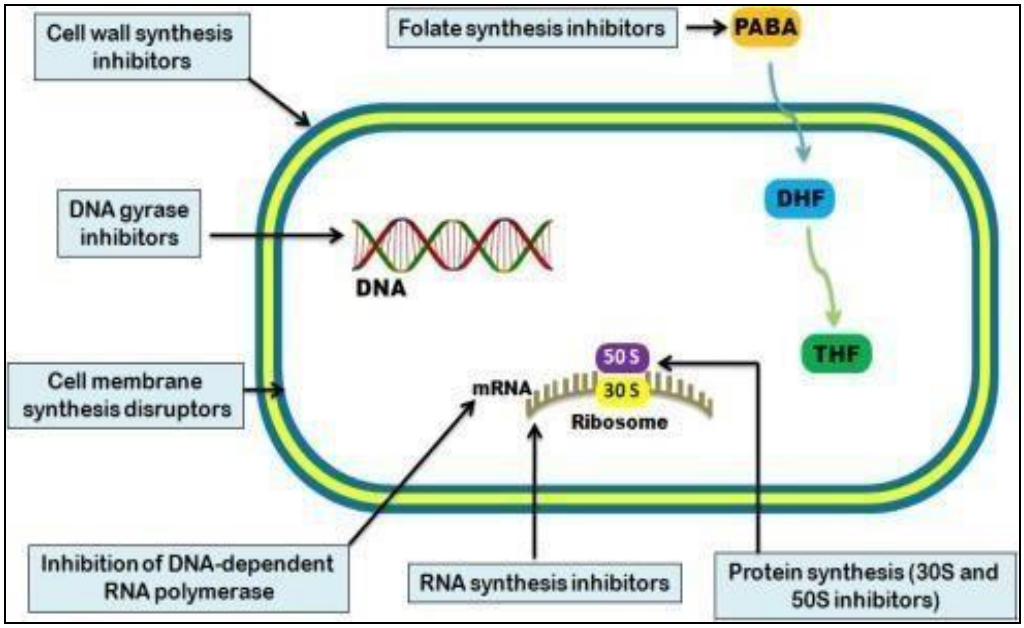

Fig 2 Mode of Action of Antibiotics [18].

Table 1 Mode of Action of Different Classes of Antibiotics [18].

Mode of action	Targets	Drug class	Specific drugs example
Cell wall synthesisinhibition	Penicillin-bindingprotein	β-lactams	Penicillin G, amoxicillin, and cephalosporin C
	Peptidoglycan Subunits	Glycopeptides	Vancomycin
Inhibition of proteinsynthesis	30 s subunit	Aminoglycosides and tetracyclines	Streptomycin, gentamicin, neomycin,tetracycline, and doxycycline
	50 s subunit	Macrolides, chloramphenicol, and oxazolidinones	Erythromycin, azithromycin, chloramphenicol, and linezolid

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Inhibition of nucleicacid synthesis	RNA	Rifamycin	Rifampin
	DNA	Fluoroquinolones	Ciprofloxacin and ofloxacin
Anti-metabolites	Folic acid synthesisenzymes	Sulfonamides and trimethoprim	Sulfamethoxazole, dapsone, and trimethoprim.
Disrupt membranes	Lipopolysaccharides	Polymyxins	Polymyxin B and colistin

➢ *Antibiotics Inhibiting Cell Wall Synthesis*

Bacterial cell wall also are primarily made of a network of cross-linked peptidoglycan [19]. Besides, the significance of this lies in the vulnerability of bacterial cells to antibiotics, particularly β-lactams (like penicillin as well as its derivatives, cephalosporins, and the carbapenems) as well as glycopeptides like vancomycin. These antibiotics work by inhibiting the biosynthesis of peptidoglycan, effectively disrupting the construction of the bacterial cell wall. As an outcome of this interference, the bacterial cells become susceptible to osmotic pressure and autolysis, ultimately leading to their demise. This mode of action is highly selective because animal cells, unlike bacterial ones, do not possess peptidoglycan in their cell walls [20].

- *B-Lactam Antibiotics*

Peptidoglycans, essential elements of cell walls for bacteria that provide structural support, are present in Gram – positive as well as Gram – negative bacteria. Nevertheless, its thickness varies significantly, with Gram – positive bacteria having a thick layer of peptidoglycan composed of ten to forty layers, while Gram-negative bacteria have a thinner layer consisting of just one or two layers [21]. Peptidoglycan is primarily composed of glycan chains consists of N- acetylglucosamine (NAG) and N-acetylmuramic acid (NAM) disaccharide subunits, crosslinked bypentapeptide chains [19].

Beta-lactam antibiotics work by inhibiting the last phase of the peptidoglycan production through the acylation of transpeptidases responsible for cross – linking the peptides within the peptidoglycan structure. The primary targets of beta – lactam antibiotics are the penicillin – binding proteins (PBPs). This disruption of the terminal transpeptidation process ultimately leads to the loss of viability and lysis of the microorganisms [22].

- *Glycopeptides*

Vancomycin is a glycopeptide antibiotic that interferes with bacterial cell wall formation. It achievesthis by binding to the D-Ala-D-Ala terminal of the growing peptide chain as part of the cell wall formation process. This action of attachment, inhibits the function of the enzyme known as transpeptidase. As a consequence, the enzyme is unable to facilitate the elongation and the cross-linking of a peptidoglycan chain within the cell wall of the bacteria [23].

- *Antibiotics Inhibiting Protein Synthesis*

The bacterial ribosomes 70S are constituted of two subunits: the 30S and 50S subunits. These ribosomes are targeted by various antibiotics to inhibit protein synthesis. Aminoglycosides and Tetracyclines primarily affect the 30S subunits, while Chloramphenicol, Macrolides, and Oxazolidinones primarily target the 50S subunits [24].

➢ *Inhibitors of 30S Subunit*

- *Aminoglycosides*

Aminoglycosides, including neomycin, streptomycin, as well as gentamicin, exert their antibacterial effects by tightly binding to the A-site on the 16S ribosomal RNA (rRNA) within the 30S ribosomal subunit. This interaction leads to a unique mechanism where these antibiotics promote the codons misreading during the delivery of aminoacyl-transfer RNA. As a consequence, incorrect amino acids are incorporated into the growing polypeptide chain. Eventually, this aberrant protein synthesis results in the release of defective proteins, which can have detrimental effects on the integrity of the cell membrane [24].

- *Tetracyclines*

Tetracycline antibiotics operate by freely diffusing through porin channels in the bacterial cell membrane. Once inside the cell, they establish reversible bonds with the 30S ribosomal subunit. This interaction effectively impedes the process of polypeptide synthesis by obstructing the binding of transfer RNA (tRNA) to the mRNA-ribosome complex [25].

➢ *Inhibitors of 50S Subunit*

- *Macrolides*

Macrolides, such as azithromycin, attach to the 23S rRNA of bacterial 50S ribosomal subunits. They inhibit the translocation process or transpeptidation of protein synthesis, inducing during the premature separation of non-complete peptide chains, preventing bacterial protein synthesis [26].

- *Chloramphenicol*

As chloramphenicol is lipid-soluble, it reveals, with good absorption properties *in vivo* and it can pass through bacterial cell membranes. It then attaches, reversibly to the L16 protein of the 50S subunit of bacterial ribosomes, inhibiting peptide bond formation and resulting protein synthesis by preventing amino acid transfer to expand peptide chains, possibly by suppressing peptidyl transferase activity [27].

- *Oxazolidinones*

Oxazolidinones, such as linezolid and tedizolid work as an antibacterial medicine by interfering with the bacterial proteins translation. They connect to a site on the 50S subunit of the bacterial 23S ribosomal RNA, preventing the development of a functional 70S initiation complex, which is needed for bacterial multiplication, and thus preventing bacteria from reproducing [28].

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➢ *Antibiotics Inhibiting Nucleic Acid Synthesis*

Some of the antibacterial medicines such as Rifamycin and the Fluoroquinolones activity through hindering RNA and DNA, correspondingly [29].

- *Rifamycin*

Rifamycin functions by tightly binding to a specific subunit of bacterial DNA-dependent RNA polymerase deep within the DNA/RNA pathway. This interaction enables Rifamycin to directly obstruct the elongation of RNA in bacterial cells. Notably, bacterial RNA polymerase enzymes exhibit structural differences when compared to their eukaryotic counterparts. These distinctions are crucial because they confer selective toxicity, allowing Rifamycin to target bacterial cells [29, 30].

- *Fluoroquinolones*

Quinolones are a class of antibiotics that disrupt DNA synthesis by targeting two essential enzymesknown as DNA gyrase and topoisomerase IV, both of which belong to the type II topoisomerase family. These enzymes play a crucial activity in allowing one double-stranded DNA molecule to pass through another, followed by the subsequent relegation of the original strand. Quinolones exhibit a strong binding affinity for the A subunit of DNA gyrase. This binding interferes with the enzyme's ability to split and reseal DNA strands, thereby disrupting its normal function and impeding the process of cell division [31].

In the context of Gram-positive bacteria, the primary target of quinolones is topoisomerase IV. Thisenzyme plays a pivotal role in nicking and separating the daughter DNA strands following DNA replication. Quinolones with a higher affinity for topoisomerase IV are more potent against Gram- positive bacteria, making them effective in combating infections caused by such bacterial strains. In contrast, in other bacteria, DNA gyrase is the primary target of quinolones, and their affinity for the A subunit of this enzyme is instrumental in disrupting the normal functioning of DNA gyrase [32].

➢ *Inhibition of Metabolic Pathways*

Certain synthetic antibiotics, such as sulfonamides and trimethoprim, are known to act as anti- metabolites by competitively inhibiting specific enzymes in the bacterial metabolic pathways. These inhibitory actions on bacterial enzymes are crucial in managing and controlling bacterial infections [33].

- *Sulfonamides*

Sulfonamides hinder bacterial growth by interfering with the production of tetrahydro-folic acid (THF), which is vital for processes like purine and dTMP synthesis. This interference occurs by competing with the para-aminobenzoic acid (PABA) for attaching towards dihydrofolate synthetase, an essential stage in the conversion of pteridine and PABA into dihydropteroic acid [34].

- *Trimethoprim*

Trimethoprim functions by effectively inhibiting the activity of dihydrofolate reductase, a crucial enzyme responsible for catalyzing the transformation of the dihydrofolate (DHF) into tetrahydrofolate (THF). Tetrahydrofolate is essential for various bacterial processes, including the synthesis of proteins as well as nucleic acids, which are vital for the bacterial survival. Consequently, the inhibition of THF synthesis has a bactericidal effect [33, 35].

In some cases, Trimethoprim is utilized in association with sulfamethoxazole, a sulfonamide. Sulfamethoxazole plays a role in preventing an earlier stage in bacterial protein production. When employed together, sulfamethoxazole and the trimethoprim collectively hinder two distinct phases in bacterial nucleic acid as well as protein biosynthesis. While Trimethoprim alone exhibits bacteriostatic properties, the combination of sulfamethoxazole and trimethoprim is thoughtto possess bactericidal effects [35].

➢ *Inhibition of Cell Membrane Function*

Polymyxins, including polymyxin B and polymyxin E, belong to a specific group of antibiotics thathave the unique ability to disrupt the cell membranes of bacteria [36]. These antibiotics are characterized by their detergent-like, lipophilic properties, and they operate through interfering with lipopolysaccharide component found in Gram-negative bacteria [37, 38, 39].

VI. MECHANISMS OF ANTIBIOTICS RESISTANCE

Antibiotic resistance exists in two primary forms: innate (naturally occurring in organisms) and acquired (developed following antibiotic exposure) [38]. Innate resistance can be either constitutive or facilitated by genes usually present, but activated in the bacterial cell, in response to antibiotics. On the other hand, acquired resistance results from bacterial genetic material acquisition throughprocesses like translation, conjugation, transposition, or mutations in the bacteria's own DNA [37, 40]. Antimicrobial resistance mechanisms are grouped into four main types: (1) restriction of drug uptake, (2) modification of the drug targets, (3) in activation of the drugs, and (4) drug efflux. In developing countries, infections remain a significant cause of mortality, largely driven by the emergence of new infectious agents and, more critically, antimicrobial resistance. Bacteria have evolved in response to the indiscriminate use of antibiotics, rendering these agents less effective. Consequently, AMR is known as a major challenge in treating microbial infections. Bacteria employ various biochemical resistance mechanisms, including antibiotic inactivation, modification of drug targets, altered permeability, as well as the "bypass" of metabolic pathways. Assessing bacterial resistance towards antibiotics across all classes (the phenotypes) as well as identifying genetic mutations accountable for the resistance (genetic analysis) are valuable strategies. A deeper understanding of antibiotic resistance mechanisms can assist clinicians in making informed decisions regarding antibiotic use in different clinical scenarios. This review explores the mechanisms of action as well as the development of resistance in commonly employed antibiotics [18]. Gram – negative bacteria have the

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capacity to utilize all four resistance mechanisms, whereas Gram-positive bacterial are lesser likelyto limit drug-uptake (due to the absence of lipopolysaccharides within the outer membrane) and usedrug efflux mechanisms [41].

➢ *Limiting Drug-Uptake*

Gram – negative bacteria possess a natural defense mechanism against certain antibiotics that is rooted in the impermeable nature of their outer membrane, which is fortified by a lipopolysaccharide (LPS)layer. This protective outer structural cell-membrane hinders the penetration of antibiotics, as exemplified by the inefficacy of glycopeptide antibiotics like vancomycin against the Gram – negative bacteria. This is largely because of their incapability to traverse the outer membrane barrier. The outer structural cell-membrane's altered permeability also affects hydrophilic molecules like β-lactams, tetracyclines, and specific fluoroquinolones. The outer bacterial-membrane can undergo modifications that impact its permeability, making it harder for these antibiotics to access the bacterial cells. Additionally, certain mechanisms come into play for particular bacterial species, such as enterococci, where porin channels are downregulated or replaced with non-selective channels, rendering them intrinsically tolerant to aminoglycosides. Furthermore, research indicates that a reduction in porin expression plays a substantial role in drug resistance, particularly for antibiotics like carbapenems, in member of the Enterobacterales order, *Pseudomonas spp* and *Acinetobacter spp*. In these cases, resistance to the carbapenems can arise even in the absence of carbapenemase enzymes, as mutations that decrease porin induction or the presence of mutated porin alleles can confer resistance. Another strategy employed by bacteria to defend against antibiotics is biofilm formation. Bacteria can form biofilms, which consist of a matrix containing polysaccharides, proteins, and DNA. This matrix acts as a shield that restricts the penetration of antimicrobial agents into the bacterial cells, enhancing the bacteria's resistance and facilitating colonization [42, 43, 44, 45].

➢ *Drug Efflux*

Bacterial efflux pumps play a noteworthy function in inner resistance of the Gram-negative bacteria, actively expelling many antibiotics from the cell. These pumps come in diverse chaps within most bacteria, and they are categorized into five primary families centered on their structure as well as energy sources. The five primary efflux pump families are the ATP-binding cassette (ABC) family, Multi-drug and Toxic Compound Extrusion (MATE) family, small multidrug resistance (SMR) family, resistance – nodulation – cell division (RND) family, as well as large facilitator superfamily (MFS) [38]. Notably, the RND family differs from the others as it functions as a multi-part pump that transports substances through the cell envelope, while the remaining families are single pumps responsible for moving substrates across the cytoplasmic membrane [6]. One classic example of efflux-mediated resistance is observed in tetracycline resistance, where Tet efflux pumps (belonging to the MFS family) utilize proton transfer as an energy source to remove tetracyclines. Furthermore, several multidrug resistance (MDR) efflux pumps, like MexAB-OprM in Pseudomonas aeruginosa and the AcrAB-TolC in Enterobacterales (RND family members), can also expel tetracyclines as part of their contributions to multidrug resistance [25]. Efflux- mediated resistance also extends to macrolide antibiotics. The mef genes, known for expelling macrolides like erythromycin, are the most extensively studied efflux pumps for this class of antibiotics. Additionally, the ABC family member MacB functions as a tripartite pump (MacAB- TolC) for the extrusion of macrolide drugs [6].

➢ *Drug Inactivation*

Bacteria inactivate the antibiotic through one or two ways: first, by destroying the drug, or even by the chemical alterations of the drug [42].

➢ *Chemical Modification of the Drug*

Bacteria have the capacity to produce enzymes that may link to numerous chemical sets to drugs, preventing antibiotics product effectively attaching to their intended targets within the bacterial cell. This process involves the transfer of acetyl, phosphoryl, and the adenyl groups to the drug compounds and is recognized as one of the most effective mechanisms for rendering drugs inactive through chemical group transfer. Acetylation is a frequently utilized method for this purpose, and it is associated with drugs such as aminoglycosides, chloramphenicol, streptogramins, and fluoroquinolones. Specifically, aminoglycosides are known to be targeted through adenylation as well as phosphorylation processes. These aminoglycoside modifying enzymes (AMEs) play a crucialrole in covalently modifying hydroxyl or amino groups on the aminoglycoside molecules, renderingthem inactive. This serves as a prominent example of how bacteria develop resistance to the drugs via the modification of the drug molecules [46, 6].

➢ *Destroying the Drugs*

Penicillin and cephalosporins are widely used antimicrobial agents, with a crucial structural featureknown as the β-lactam loop that is common to all members of this drug class.The mainchallenge to the effectiveness of these β-lactam drugs is the action of β-lactamases, which function to break down the β-lactam loop. This enzymatic process essentially destroys the critical β-lactam ring structure, ultimately preventing these antibiotics from to bind to the penicillin-binding proteins (PBSs) [20].

➢ *Drug Target Modification*

Bacteria develop resistance to antibiotics through various mechanisms, and one common approach involves altering the antibiotic's target [38]. For instance, changes in the number and arrangement of penicillin-binding proteins (PBPs) can lead to resistance against β-lactam drugs, affecting the drug's capability to bind to its target [20]. In some cases, structural modifications, like the developments of a mecA gene in *S. aureus*, can completely hinder drug binding [47]. Another example of antibiotic resistance is found in the erythromycin ribosome methylase (erm) gene family. These genes methylate 16S rRNA, altering the drug-binding site and preventing macrolides, streptogramins, as well as lincosamines from binding effectively [48].

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Resistance to antibiotics that inhibit synthesis of the nucleic acid, such as fluoroquinolones, occurs through mutations that change DNA gyrase or topoisomerase IV, resulting in modifications to these components and reducing the drug's ability to bind to them [32].

VII. GLOBAL ACTION TO RESIST ANTIMICROBIAL RESISTANCE

The well-being and survival of people in developed nations have seen significant improvements thanks to the availability of antibiotics, safe water, hygiene practices, and vaccinations. The primary challenge lies in extending the accessibility of antibiotics to developing countries while preventing the widespread development of antimicrobial resistance, which could have catastrophic consequences. Despite efforts to reduce antibiotic usage, there remains a pressing the need of new antibiotics development. However, it is equally important to focus on advancements in diagnostics, vaccinations, and infection prevention strategies through innovative formulation and distribution methods in order to reduce the reliance on antibiotics. The introduction of new vaccines, for instance, can help reduce the demand for antibiotics [49].

- *Emergence of Resistance Among UTI Pathogens*

Over the last thirty years, a quite number of studies were initiated to substantiate the growing resistance of UTIs causing pathogens. The report available confirms that the surge in resistance towards frequently used antibacterial-drugs is the direct result of non-appropriated antimicrobial agent utilization. The explosion resistance in UTIs' pathogens is a pressing concern that requires immediate attention to find effective solutions. It's worth noting that the nature and extent of treatment can vary significantly between different groups of patients. For instance, women of reproductive age, pregnant women, and elderly individuals in long-term care have contrasting treatment needs. Pregnant women, in particular, have revealed an increasing prevalence of Gram – negative bacteria with multidrug resistance, raising concerns about the extent of antimicrobial resilience in these pathogens. When it comes to elderly and non-pregnant women with asymptomatic bacteriuria, the benefits of treatment appear limited, but there's a strong insistence on conducting screening before prescribing antimicrobial agents [50]. One of the major global issue is the widespread antimicrobial resistance exhibited by UTI pathogens against commonly used drugs. This resistance pattern varies relating on factors like the site of infection, infectious area conditions, and the stage of infection. Many healthcare facilities in developing nations depend on the strip urinalysis to assess urine samples from pregnant women. However, this method often fails to provide an accurate diagnosis of the infection, leading to the inappropriate use of antimicrobial agents and empirical practices, a significant contributor to antibiotic resistance in UTI pathogens. Numerous research studies have highlighted the resistance of Gram-negative pathogens towards commonly prescribed beta-lactam antibiotics such as amoxicillin and ampicillin, with some pathogens displaying multidrug resistance. Previous research has consistently demonstrated shifts in the antimicrobial susceptibility patterns of UTI-causing pathogens. A study focused on pregnant women during their initial prenatal visit revealed the presence of pathogens with multidrug resistance [51, 52].

Pathogens such as *P. aeruginosa*, *E. coli*, *Klebsiella* spp as well as *Proteus* species are exponentially resistant to the antibiotics like cotrimoxazole and ampicillin.

Moreover, there are concerns about the ineffectiveness of antibiotics such as cefotaxime and ciprofloxacin when dealing with *P. aeruginosa*, a pathogen that is less commonly associated with urinary tract infections (UTIs) compared to more typical culprits like *Escherichia coli* and *Staphylococcus* species. This suggests a growing trend of resistance among major UTI-causing pathogens, making them increasingly resilient to commonly used antimicrobial agents. Notably, accounting for 80% of cases, the contribution of other diseases cannot be dismissed. One such pathogen gaining importance in UTIs is *S. aureus*, which has been a cause for concern due to its growing resistance to antimicrobial agents. Various studies have investigated the antibacterial patterns of *S. aureus*, especially among pregnant females during the antenatal visits. These investigations have established the roles of this pathogen in multiplying within the intestines and vagina and its association with asymptomatic UTIs and non-complicated infections of the skin. Surprisingly, the appearance of UTIs, attributed to Staphylococcal infections, has been reported in both gravid and non-gravid women, with the presence of Multidrug-Resistant, *S. aureus* becoming increasingly prevalent. It is worth noting that within the *Staphylococcus genus*, over 30 species have been identified, but *S. aureus* stands out as the most virulent strain with well-established pathogenicity [53].

Several researchers have provided evidence to establish the role of *S. aureus* in causing both healthcare and community-associated infections [54, 55]. The antimicrobial susceptibility patterns of *S. aureus* varied among different sites, and the resistance exhibited by pathogens separated from the reproductive tract varied from those isolated from other locations [56, 57]. In the infections' context, *S. aureus* has been observed to outcompete *E. coli* and Klebsiella, with a predominant population of *S. aureus* present [58, 59]. Researcher have revealed that *S. aureus* colonization among pregnant women can influence the health of neonates born to these mothers, and demographic factors such as maternal health, gestational age, parity, gravidity, socio-economic status, and previous infection history play an important function in the infection's development [60]. It is worth noting that some studies suggest that other Staphylococcal species are sometimes misidentified as *S. aureus* but are also capable of causing infections [61, 62]. *S. aureus* colonization during gravid-state has been associated with increased morbidity and mortality rates, and the resistance pattern of *S. aureus* to fluoroquinolone antibiotics like ciprofloxacin, ofloxacin, and norfloxacin poses challenges for empirical treatment [63].

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➢ *Prevention and Control of Antibiotic Resistance*

- *Individuals*

Using antibiotics should always be done under the guidance of a certified healthcare professional. It is crucial not to insist on antibiotics if a healthcare provider deems them unnecessary. Infection prevention involves various measures, including practicing safe food handling, refraining from using or sharing leftover antibiotics, maintaining good hand hygiene, getting recommended vaccinations, and engaging in safer sexual practices [64]. Additionally, it is advisable to avoid close contact with individuals who are unwell and adopt a healthier lifestyle.

- *Health Professional*

To prevent and oversee the proliferation of antibiotic resistance, it is imperative for healthcare practitioners to maintain cleanliness and hygiene in their equipment, hands, and immediate environment. Antibiotics should be administered and prescribed only when deemed absolutely necessary, aligning with established guidelines. It is also advisable to educate patients on the proper antibiotics consumption and the risks attributed to their misuse. Additionally, monitoring teams should be established for tracking antibiotic-resistant diseases [64].

- *Agricultural Sector*

To prevent the explosion of antimicrobial resistance (AMR) in microbes, it is necessary for antibiotics to be administered under the guidance of veterinarians. In place of antibiotic-based treatments, vaccinations should be prioritized as the primary option [64].

- *Policymakers*

To prevent the exponential appearance of antimicrobial-resistant (AMR) microbes, it is essential for policymakers to enhance existing policies, effectively implement infection prevention strategies, and ensure the accessibility of information [64].

- *Healthcare Sector*

To combat the challenge of AMR, it's imperative for the health-care sector to allocate resources towards extensive research and development efforts. This should encompass the creation of vaccines, diagnostic tools, novel pharmaceuticals, and other innovative methods aimed at preventing and monitoring the proliferation of AMR [64].

VIII. CONCLUSION

Antibiotic resistance in Urinary tract infections accounts among significant causes of morbi – mortality worldwide. A very large list of antibiotics is known. But, many factors like antibiotic abuse, unsuitable prescription, inaccurate diagnosis, lower concentrated antibiotics, etc. may contribute to this phenomenon of antibiotic resistance through the world.

RECOMMENDATIONS

➢ UTI screening should be done for earlier treatment of Urinary Tract Infections in order to avoid UTIs' complications, and clinicians should take in consideration UTI screening results while prescribing antibiotics;
➢ Good strategies of sensitization should be implemented about advantages and disadvantages of antibiotic treatment since self-medication / antibiotic abuse has been shown as one of factors leading to antibiotic resistance.

REFERENCES

[1]. CDC. (2022). *Suffering from a urinary tract infection?* Centers for Disease Control and Prevention. https://www.cdc.gov/antibiotic-use/uti.html
[2]. Tessema, N. N., Ali, M. M., & Zenebe, M. H. (2020). Bacterial associated urinary tract infection, risk factors, and drug susceptibility profile among adult people living with HIV at Haswassa University Comprehensive Specialized Hospital, Hawassa, Southern Esthiopia. *Scientific Reports*, 10(1):1–9. https://doi.org/10.1038/s41598-020-67840-7
[3]. Kostakioti, M., Hultgren, S. J., & Hadjifrangiskou, M. (2012). Molecular blueprint of uropathogenic Escherichia coli virulence provides clues toward the development of anti- virulence therapeutics. *Virulence*, *3*(7), 592–594. https://doi.org/10.4161/viru.22364
[4]. Jancel, T., & Dudas, V. (2002). Management of uncomplicated urinary tract infections. *The Western Journal of Medicine*, *176*(1), 51–55. https://doi.org/10.1136/ewjm.176.1.51
[5]. Gupta, K., Hooton, T. M., Roberts, P. L., & Stamm, W. E. (2001). Patient-initiated treatment of uncomplicated recurrent urinary tract infections in young women. *Annals of Internal Medicine*, *135*(1), 9–16. https://doi.org/10.7326/0003-4819-135-1-200107030-00004
[6]. Munita, J. M., & Arias, C. A. (2016). Mechanisms of Antibiotic Resistance. In *Virulence Mechanisms of Bacterial Pathogens* (pp. 481–511). John Wiley & Sons, Ltd. https://doi.org/10.1128/9781555819286.ch17
[7]. Sreeja M.K., Gowrishankar N.L., Adisha S., Divya K.C. (2017). Antibiotic Resistance-Reasons and the Most Common Resistant Pathogens – A Review. *Research Journal of Pharmacy and Technology*, *10*(6), 1886–1890. https://doi.org/10.5958/0974-360X.2017.00331.6
[8]. Mahmoud, M. A., Aldhaeefi, M., Sheikh, A., & Aljadhey, H. (2018). Community pharmacists perspectives about reasons behind antibiotics dispensing without prescription: A qualitative study. *BiomedicalResearch*, *29*(21). https://doi.org/10.4066/biomedicalresearch.29-18-1112
[9]. Chokshi, A., Sifri, Z., Cennimo, D., & Horng, H. (2019). Global Contributors to Antibiotic Resistance.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26feb272

Journal of Global Infectious Diseases, *11*(1), 36–42. https://doi.org/10.4103/jgid.jgid_110_18

[10]. Wintersdorff Von, C. J. H., Penders, J., van Niekerk, J. M., Mills, N. D., Majumder, S., van Alphen, L. B., Savelkoul, P. H. M., & Wolffs, P. F. G. (2016). Dissemination of Antimicrobial Resistance in Microbial Ecosystems through Horizontal Gene Transfer. *Frontiers in Microbiology*, *7*, 173. https://doi.org/10.3389/fmicb.2016.00173

[11]. Holmes, A. H., Moore, L. S. P., Sundsfjord, A., Steinbakk, M., Regmi, S., Karkey, A., Guerin, P.J., & Piddock, L. J. V. (2016). Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet (London, England)*, *387*(10014), 176–187. https://doi.org/10.1016/S0140-6736(15)00473-0

[12]. Martínez, J. L., Coque, T. M., & Baquero, F. (2015). What is a resistance gene? Ranking risk in resistomes.*Nature Reviews.Microbiology*, *13*(2), 116–123.https://doi.org/10.1038/nrmicro3399

[13]. Zhao, R., Feng, J., Liu, J., Fu, W., Li, X., & Li, B. (2019). Deciphering of microbial community and antibiotic resistance genes in activated sludge reactors under high selective pressure of different antibiotics. *Water Research*, *151*, 388–402. https://doi.org/10.1016/j.watres.2018.12.034

[14]. Denning, D. W., Perlin, D. S., Muldoon, E. G., Colombo, A. L., Chakrabarti, A., Richardson, M. D., & Sorrell, T. C. (2017). Delivering on Antimicrobial Resistance Agenda Not Possible without Improving Fungal Diagnostic Capabilities. *Emerging Infectious Diseases*, *23*(2), 177–183. https://doi.org/10.3201/eid2302.152042

[15]. Ventola, C. L. (2015). The antibiotic resistance crisis: Part 1: causes and threats. *P & T: A Peer-Reviewed Journal for Formulary Management*, *40*(4), 277–283.

[16]. Marc, C., Vrignaud, B., Levieux, K., Robine, A., Guen, C. G.-L., & Launay, E. (2016). Inappropriate prescription of antibiotics in pediatric practice: Analysis of the prescriptions in primary care. *Journal of Child Health Care: For Professionals Working with Children in the Hospital and Community*, *20*(4), 530–536. https://doi.org/10.1177/1367493516643421

[17]. Almagor, J., Temkin, E., Benenson, I., Fallach, N., Carmeli, Y., & DRIVE-AB consortium. (2018). The impact of antibiotic use on transmission of resistant bacteria in hospitals: Insights from an agent-based model. *PloS One*, *13*(5), e0197111. https://doi.org/10.1371/journal.pone.0197111

[18]. Kapoor, G., Saigal, S., & Elongavan, A. (2017). Action and resistance mechanisms of antibiotics: A guide for clinicians. *Journal of Anaesthesiology, Clinical Pharmacology*, *33*(3), 300–305. https://doi.org/10.4103/joacp.JOACP_349_15

[19]. Levin, P. A., & Angert, E. R. (2015). Small but Mighty: Cell Size and Bacteria. *Cold Spring Harbor Perspectives in Biology*, *7*(7), a019216. https://doi.org/10.1101/cshperspect.a019216

[20]. Bush, K., & Bradford, P. A. (2016). β-Lactams and β-Lactamase Inhibitors: An Overview. *Cold Spring Harbor Perspectives in Medicine*, *6*(8), a025247. https://doi.org/10.1101/cshperspect.a025247 CDC. 2013.

[21]. Prochnow-Mai, A., Clauson, M., Hong, J., & Murphy, A. B. (2016). Gram positive and Gram negative bacteria differ in their sensitivity to cold plasma. *Scientific Reports*, *6*, 38610. https://doi.org/10.1038/srep38610

[22]. Page, M. G. P. (2012). Beta-Lactam Antibiotics. In T. J. Dougherty & M. J. Pucci (Eds.), *Antibiotic Discovery and Development* (pp. 79–117). Springer US. https://doi.org/10.1007/978-1- 4614-1400-1_3

[23]. Wang, F., Zhou, H., Olademehin, O. P., Kim, S. J., & Tao, P. (2018). Insights into Key Interactions between Vancomycin and Bacterial Cell Wall Structures. *ACS Omega*, *3*(1), 37–45. https://doi.org/10.1021/acsomega.7b01483

[24]. Krause, K. M., Serio, A. W., Kane, T. R., & Connolly, L. E. (2016). Aminoglycosides: An Overview. *Cold Spring Harbor Perspectives in Medicine*, *6*(6), a027029. https://doi.org/10.1101/cshperspect.a027029

[25]. Grossman, T. H. (2016). Tetracycline Antibiotics and Resistance. *Cold Spring Harbor Perspectives in Medicine*, *6*(4), a025387. https://doi.org/10.1101/cshperspect.a025387

[26]. Parnham, M. J., Erakovic Haber, V., Giamarellos-Bourboulis, E. J., Perletti, G., Verleden, G. M., & Vos, R. (2014). Azithromycin: Mechanisms of action and their relevance for clinical applications. *Pharmacology & Therapeutics*, *143*(2), 225–245. https://doi.org/10.1016/j.pharmthera.2014.03.003

[27]. Dinos, G. P., Athanassopoulos, C. M., Missiri, D. A., Giannopoulou, P. C., Vlachogiannis, I. A., Papadopoulos, G. E., Papaioannou, D., & Kalpaxis, D. L. (2016). Chloramphenicol Derivatives as Antibacterial and Anticancer Agents: Historic Problems and Current Solutions. *Antibiotics (Basel, Switzerland)*, *5*(2), 20. https://doi.org/10.3390/antibiotics5020020

[28]. Papich M.G., & Linezolid. (2016). *Saunders handbook of veterinary drugs.* Docer.com.ar. https://docer.com.ar/doc/xcvvx1s

[29]. Bhattacharjee, M. (2016). *Antibiotics That Inhibit Nucleic Acid Synthesis* (pp. 109–128). https://doi.org/10.1007/978-3-319-40746-3_5

[30]. Saito, K., Warrier, T., Somersan-Karakaya, S., Kaminski, L., Mi, J., Jiang, X., Park, S., Shigyo, K., Gold, B., Roberts, J., Weber, E., Jacobs, W. R., & Nathan, C. F. (2017). Rifamycin action on RNA polymerase in antibiotic-tolerant Mycobacterium tuberculosis results in differentially detectable populations. *Proceedings of the National Academy of Sciences ofthe United States of America*, *114*(24), E4832–E4840. https://doi.org/10.1073/pnas.1705385114

[31]. Aldred, K. J., Kerns, R. J., & Osheroff, N. (2014). Mechanism of quinolone action and resistance. *Biochemistry*, *53*(10), 1565–1574. https://doi.org/10.1021/bi5000564

[32]. Nainu F., A. Masyita, M.A. Bahar, M. Raihan, S.R. Prova, S. Mitra, & et al., (2021). *Pharmaceutical*

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26feb272

Prospects of Bee Products: Special Focus on Anticancer, Antibacterial, Antiviral, and Antiparasitic Properties—PubMed. https://pubmed.ncbi.nlm.nih.gov/34356743/

[33]. Fernández-Villa, D., Aguilar, M. R., & Rojo, L. (2019). Folic Acid Antagonists: Antimicrobial and Immunomodulating Mechanisms and Applications. *International Journal of Molecular Sciences*, *20*(20), 4996. https://doi.org/10.3390/ijms20204996

[34]. Akter, T., Shahriar, A., Rahman, T., Mahmud, M. R., Alo, M., & Emran, T. B. (2020). Survival Assessment of pathogenic bacteria with antibiotic resistance traits from fresh summer royal grape: In Vitro microbial challenge test. *Journal of Microbiology, Biotechnology and Food Sciences*, *10*(3), 344–349. https://doi.org/10.15414/JMBFS.2020.10.3.344-349

[35]. Wróbel, A., Maliszewski, D., Baradyn, M., & Drozdowska, D. (2019). Trimethoprim: An Old Antibacterial Drug as a Template to Search for New Targets. Synthesis, Biological Activity and Molecular Modeling Study of Novel Trimethoprim Analogs.*Molecules (Basel, Switzerland)*, *25*(1), 116. https://doi.org/10.3390/molecules25010116

[36]. Poirel, L., Jayol, A., & Nordmann, P. (2017). Polymyxins: Antibacterial Activity, Susceptibility Testing, and Resistance Mechanisms Encoded by Plasmids or Chromosomes. *Clinical Microbiology Reviews*, *30*(2), 557–596. https://doi.org/10.1128/CMR.00064-16

[37]. Lerminiaux, N. A., & Cameron, A. D. S. (2019). Horizontal transfer of antibiotic resistance genes in clinical environments. *Canadian Journal of Microbiology*, *65*(1), 34–44. https://doi.org/10.1139/cjm-2018-0275

[38]. Reygaert, W. C. (2018). An overview of the antimicrobial resistance mechanisms of bacteria. *AIMS Microbiology*, *4*(3), 482–501. https://doi.org/10.3934/microbiol.2018.3.482

[39]. Trimble, M. J., Mlynárčik, P., Kolář, M., & Hancock, R. E. W. (2016). Polymyxin: Alternative Mechanisms of Action and Resistance. *Cold Spring Harbor Perspectives in Medicine*, *6*(10), a025288. https://doi.org/10.1101/cshperspect.a025288n

[40]. Culyba, M. J., Mo, C. Y., & Kohli, R. M. (2015). Targets for Combating the Evolution of Acquired Antibiotic Resistance. *Biochemistry*, *54*(23), 3573–3582. https://doi.org/10.1021/acs.biochem.5b00109

[41]. Hoffman, S. B. (2001). *Mechanisms of Antibiotic Resistance*. Compendium on Continuing Education for the Practising Veterinarian -North American Edition- 23(5):464-472

[42]. Blair, J. M. A., Webber, M. A., Baylay, A. J., Ogbolu, D. O., & Piddock, L. J. V. (2015). Molecular mechanisms of antibiotic resistance. *Nature Reviews. Microbiology*, *13*(1), 42–51. https://doi.org/10.1038/nrmicro3380

[43]. Iredell, J., Brown, J., & Tagg, K. (2016). Antibiotic resistance in Enterobacteriaceae: Mechanisms and clinical implications. *BMJ (Clinical Research Ed.)*, *352*, h6420. https://doi.org/10.1136/bmj.h6420

[44]. Pang, Z., Raudonis, R., Glick, B. R., Lin, T.-J., & Cheng, Z. (2019). Antibiotic resistance in Pseudomonas aeruginosa: Mechanisms and alternative therapeutic strategies. *Biotechnology Advances*, *37*(1), 177–192. https://doi.org/10.1016/j.biotechadv.2018.11.013

[45]. Hall, C. W., & Mah, T.-F. (2017). Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. *FEMS Microbiology Reviews*, *41*(3), 276–301. https://doi.org/10.1093/femsre/fux010

[46]. Lin, J., Nishino, K., Roberts, M. C., Tolmasky, M., Aminov, R. I., & Zhang, L. (2015). Mechanisms of antibiotic resistance. *Frontiers in Microbiology*, *6*, 34. https://doi.org/10.3389/fmicb.2015.00034

[47]. Foster, T. J. (2017). Antibiotic resistance in Staphylococcus aureus. Current status and future prospects. *FEMS Microbiology Reviews*,*41*(3), 430–449.https://doi.org/10.1093/femsre/fux007

[48]. Peterson, E., & Kaur, P. (2018). Antibiotic Resistance Mechanisms in Bacteria: Relationships Between Resistance Determinants of Antibiotic Producers, Environmental Bacteria, and Clinical Pathogens. *Frontiers in Microbiology*, *9*, 2928. https://doi.org/10.3389/fmicb.2018.02928

[49]. Gelband, H., & Laxminarayan, R. (2015). Tackling antimicrobial resistance at global and local scales. *Trends in Microbiology*, *23*(9), 524–526. ttps://doi.org/10.1016/j.tim.2015.06.005

[50]. Lentz GM. (2009). *Urinary Tract Infections in Obstetrics and Gynecology | GLOWM*. http://www.glowm.com/section-view/heading/Urinary Tract Infections in Obstetrics and Gynecology/item/118 Leopold, S. J., van Leth, F., Tarekegn, H., & Schultsz, C. (2014). Antimicrobial drug resistance among clinically relevant bacterial isolates in sub-Saharan Africa: A systematic review. *The Journal of Antimicrobial Chemotherapy*, *69*(9), 2337–2353. https://doi.org/10.1093/jac/dku176

[51]. Tadesse, E., Teshome, M., Merid, Y., Kibret, B., & Shimelis, T. (2014). Asymptomatic urinary tract infection among pregnant women attending the antenatal clinic of Hawassa Referral Hospital, Southern Ethiopia. *BMC Research Notes*, *7*, 155. https://doi.org/10.1186/1756- 0500-7-155

[52]. Manikandan S, Ganesapandian S, Singh M, & Kamaraguru A.K,. (2011). *Emerging of Multidrug Resistance Human Pathogens from Urinary Tract Infections*. https://doi.org/10.3923/crb.2011.9.15

[53]. Ugboma HAA, S. C. (2014). Prevalence and Antibiotic Susceptibility of Staphylococcus Aureus and Other Staphylococcal Infections in Pregnant Women Attending Antenatal Clinic in a Tertiary Hospital in Port Harcourt, Nigeria. *Journal of Infectious diseases. and Therapy*, *02*(01). https://doi.org/10.4172/2332-0877.1000125

[54]. David, M. Z., & Daum, R. S. (2010). Community-associated methicillin-resistant Staphylococcus

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26feb272

aureus: Epidemiology and clinical consequences of an emerging epidemic. *Clinical Microbiology Reviews*, *23*(3), 616–687. https://doi.org/10.1128/CMR.00081-09

[55]. Otto, M. (2010). Looking toward basic science for potential drug discovery targets against community-associated MRSA. *Medicinal Research Reviews*, *30*(1), 1-22. https://doi.org/10.1002/med.20160

[56]. Ilusanya, O., Adesetan, T., Egberongbe, H., & Otubushin, A. (2012). Asymptomatic Bacteriuria in Ante-Natal Patients Attending State Hopital, Ado-Ekiti, Ekiti State, Nigeria. *Current Research Journal of Biological Sciences*, *4*.

[57]. Imade, P. E., Izekor, P. E., Eghafona, N. O., Enabulele, O. I., & Ophori, E. (2010). Asymptomatic bacteriuria among pregnant women. *North American Journal of Medical Sciences*, *2*(6), 263–266. https://doi.org/10.4297/najms.2010.2263

[58]. Jimenez-Truque, N., Tedeschi, S., Saye, E. J., McKenna, B. D., Langdon, W., Wright, J. P., Alsentzer, A., Arnold, S., Saville, B. R., Wang, W., Thomsen, I., & Creech, C. B. (2012). Relationship between maternal and neonatal Staphylococcus aureus colonization. *Pediatrics*, *129*(5), e1252-1259. https://doi.org/10.1542/peds.2011-2308

[59]. Top, K. A., Buet, A., Whittier, S., Ratner, A. J., & Saiman, L. (2012). Predictors of *Staphylococcusaureus* Rectovaginal Colonization in Pregnant Women and Risk for Maternal and Neonatal Infections. *Journal of the Pediatric Infectious Diseases Society*, *1*(1), 7–15. https://doi.org/10.1093/jpids/pis001

[60]. Kurewa, N. E., Mapingure, M. P., Munjoma, M. W., Chirenje, M. Z., Rusakaniko, S., & Stray- Pedersen, B. (2010). The burden and risk factors of Sexually Transmitted Infections and Reproductive Tract Infections among pregnant women in Zimbabwe. *BMC infectious Diseases*, *10*, 127. https://doi.org/10.1186/1471-2334-10-127

[61]. Shittu, A. O., Okon, K., Adesida, S., Oyedara, O., Witte, W., Strommenger, B., Layer, F., & NübelU. (2011). Antibiotic resistance and molecular epidemiology of Staphylococcus aureus in Nigeria. *BMC Microbiology*, *11*, 92. https://doi.org/10.1186/1471-2180-11-92

[62]. Watkins, R. R., David, M. Z., & Salata, R. A. (2012). Current concepts on the virulence mechanisms of meticillin-resistant Staphylococcus aureus. *Journal of Medical Microbiology*, *61*(Pt 9), 1179–1193. https://doi.org/10.1099/jmm.0.043513-0

[63]. Cheung, G. Y. C., & Otto, M. (2010). Understanding the significance of Staphylococcus epidermidis bacteremia in babies and children. *Current Opinion in Infectious Diseases*, *23*(3), 208–216. https://doi.org/10.1097/QCO.0b013e328337fecb

[64]. Shahriar, A., Alo, M., Hossain, M. F., Emran, T. B., Uddin, M. Z., & Paul, A. (2019). Prevalenceof Multi-Drug Resistance Traits in Probiotic Bacterial Species from Fermented Milk Products in Bangladesh. *Microbiology Research Journal International*, 1–10. https://doi.org/10.9734/mrji/2019/v29i230161