Antibiotic resistance of urinary tract pathogens among wide population of Syrian patients.

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□ ABSTRACT □

The aim of this study was to evaluate the prevalence of antibiotic resistance among bacteria isolated from urine cultures of Syrian patients of different genders and age categories. The most frequently identified uropathogen in urine cultures was Escherichia coli (68%). Of the bacterial isolates, 2% were resistant to a single antibiotic, while 98% were resistant to at least two antibiotics. A significantly high in-vitro resistance rate (over 90%) was observed among bacterial isolates, particularly against Cefotaxime, Nalidixic acid, Cefexime, Cephalexin, and Cefpodoxime. Resistance rates for Cefetriaxone, Cefuroxime, and Trimethoprim-Sulfamethoxazole ranged from 70% to 80%. The resistance rates for Nitrofurantoin, Amoxicillin-Clavulanic acid, Ciprofloxacin, and Norfloxacin ranged from 37% to 60%. For some antibiotics, resistance rates remained consistently high across all age groups (Trimethoprim-Sulfamethoxazole, Cephalexin, and Cefexime), while for others, resistance rates increased with increasing patient age (Nitrofurantoin, Ciprofloxacin, and Norfloxacin). Finally, Amikacin, Gentamycin, and Imipenem demonstrated good sensitivity (over 90%) across all age groups.

Keywords: Urine Tract Infection, Antibiotic Resistance, Uropathogens, Syrian Patients.

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مقاومة المضادات الحيوية لمسببات التهاب المسالك البولية بين عدد كبير من المرضى السوريين

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□ ملخّص □

تهدف هذه الدراسة إلى تقييم انتشار مقاومة المضادات الحيوية بين البكتيريا المعزولة من عمليات زرع البول لدى مرضى سوريين من مختلف الفئات العمرية و الجنس. العامل المرض الأكثر شيوعًا في عمليات روع البول هو الإشريشيا كولاي (68٪). من بين العازلات البكتيرية، كانت 2٪ مقاومة لمضاد حيوي واحد، بينما كانت 98٪ مقاومة لمضاد حيوي واحد على الأقل. لوحظت نسبة مقاومة عالية جدًا في الاختبارات الحيوية (أكثر من 90٪) بين العازلات البكتيرية، ولا سيما ضد السيفوتاكسيم وحمض النااليديكسيك والسيفيكسيم وسيفالكسين والسيفبودوكسيم. تراوحت معدلات المقاومة للسيفترياكسون والسيفوروكسيم والتريميثوبريم–سلفاميثوكسازول بين 70٪ و 80٪. كانت معدلات المقاومة للنيتروفيورانتوين وحمض الأموكسيسيلين–كلافولانيك والسيبروفلوكساسين والنورفلوكساسين تتراوح بين 37٪ و 60٪. بالنسبة لبعض المضادات الحيوية، ظلت معدلات المقاومة مرتفعة بشكل ثابت في جميع الفئات العمرية (التريميثوبريم–سلفاميثوكسازول وسيفالكسين والسيفيكسيم)، بينما زادت معدلات المقاومة مع زيادة عمر المرضى في حالة بعض الأدوية (النيتروفيورانتوين والسيبروفلوكساسين والنورفلوكساسين). أخيرًا، أظهرت الأميكاسين والجنتاميسين والإيميبينيم حساسية جيدة (أكثر من 90٪) في جميع الفئات العمرية..

الكلمات المفتاحية: عدوى المسالك البولية، مقاومة المضادات الحيوية، العوامل المسببة لالتهاب المسالك البولية، المرضى السوريين.

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Introduction:

Urinary tract infection (UTI) is a prevalent infection affecting the human body. UTIs can be categorized as upper tract UTI, involving the ureters and kidneys, and lower tract UTI, the most common form of the infection that affects the urethra and bladder. The typical symptoms of lower UTIs include increased urinary frequency and urgency (dysuria), strong-smelling urine, cloudy or bloody urine, and persistent lower abdominal pain. In contrast, upper UTIs usually present with accompanying loin pain and fever. Bacterial identification in UTIs is a crucial step for therapeutic strategies [1,2]. UTIs are primarily caused by Escherichia coli, and other pathogens such as Enterobacter aerogenes, Klebsiella pneumoniae, Proteus mirabilis, Citrobacter, Pseudomonas aeruginosa, Enterococcus spp., and Serratia spp. [1,2,3].

Due to the high empirical use of antibiotics for the treatment of UTIs, antibacterial resistance of Enterobacteriaceae, specifically the main uropathogens Escherichia coli and Klebsiella pneumoniae, has significantly increased [4-10]. The high antibacterial resistance presence of such high antibacterial resistance renders the use of traditional antibiotics extremely limited, both in terms of dosage and administration route. This study aimed to evaluate the resistance rates to antibiotics among bacteria isolated from urine samples collected from Syrian patients [11-17].

Materials and methods:

Urine samples were collected in sterile urine containers in the laboratory. Blood and MacConkey agar plates were used to culture the urine samples and detect and identify microorganisms causing UTIs. After incubating the urine samples at 37°C for 24 hours, colony-forming units (CFUs) were counted. If the CFUs were greater than 100,000/mL, antibiotic sensitivity tests were carried out using Mueller Hinton Agar (MHA). The level of antibiotic susceptibility of the bacteria was determined by measuring the zone of inhibition. The antibiotics discs used in the study included Amikacin 30 µg, Gentamycin 10 µg, Nitrofurantoin 300 µg, Ceftriaxone 30 µg, Ciprofloxacin 30 µg, Imipenem 10 µg, Nalidixic acid 30 µg, Norfloxacin 10 µg, Cefpodoxime 30 µg, Cefuroxime 30 µg, Cefotaxime 30 µg, Cephalexin 30 µg, Cefixime 5 µg, Amoxicillin-clavulanic acid 30 µg, and Trimethoprim-Sulfamethoxazole 75 µg.

Results:

Between August 2022 and June 2023, 185 urine samples were collected from Syrian patients with UTIs. The samples were classified according to the patient's age and divided into two groups: group 1 (below 18 years of age) and group 2 (over 18 years of age). Among the studied UTI patients, the percentage of adult patients was higher (70%) than pediatric patients (30%). Urine samples collected from Syrian patients with UTIs were analyzed to identify the uropathogens responsible for the infection.

Escherichia coli was found to be the primary cause of UTIs (68%), followed by Klebsiella pneumoniae (24%) and other bacteria such as Enterobacter and beta-hemolytic streptococcus (8%).

The susceptibility of the isolated urine bacteria was tested against fifteen antibacterial drugs, including Amikacin, Gentamycin, Nitrofurantoin, Ceftriaxone, Ciprofloxacin, Imipenem, Nalidixic acid, Norfloxacin, Cefpodoxime, Cefuroxime, Cephalexin, Cefexime, Amoxicillin-Clavulanic acid, Trimethoprim-Sulfamethoxazole, and Cefotaxime.

Susceptibility results

Figure 1 shows the susceptibility results of 185 bacterial isolates tested against 15 antibiotics. All urine bacterial isolates were highly sensitive to Amikacin (100%), Imipenem (98%), and Gentamicin (89%). The percentage of sensitivity for urine bacterial isolates was high for Nitrofurantoin (61%), Ciprofloxacin (50%), Amoxicillin-Clavulanic acid (44%), and Norfloxacin (41%). The percentage of sensitivity for urine bacterial isolates was low for Ceftriaxone (32%), Cefuroxime (18%), Trimethoprim-Sulfamethoxazole (18%), Cephalexin (17%), Nalidixic acid (11%), Cefotaxime (9%), Cefpodoxime (9%), and Cefixime (6%).

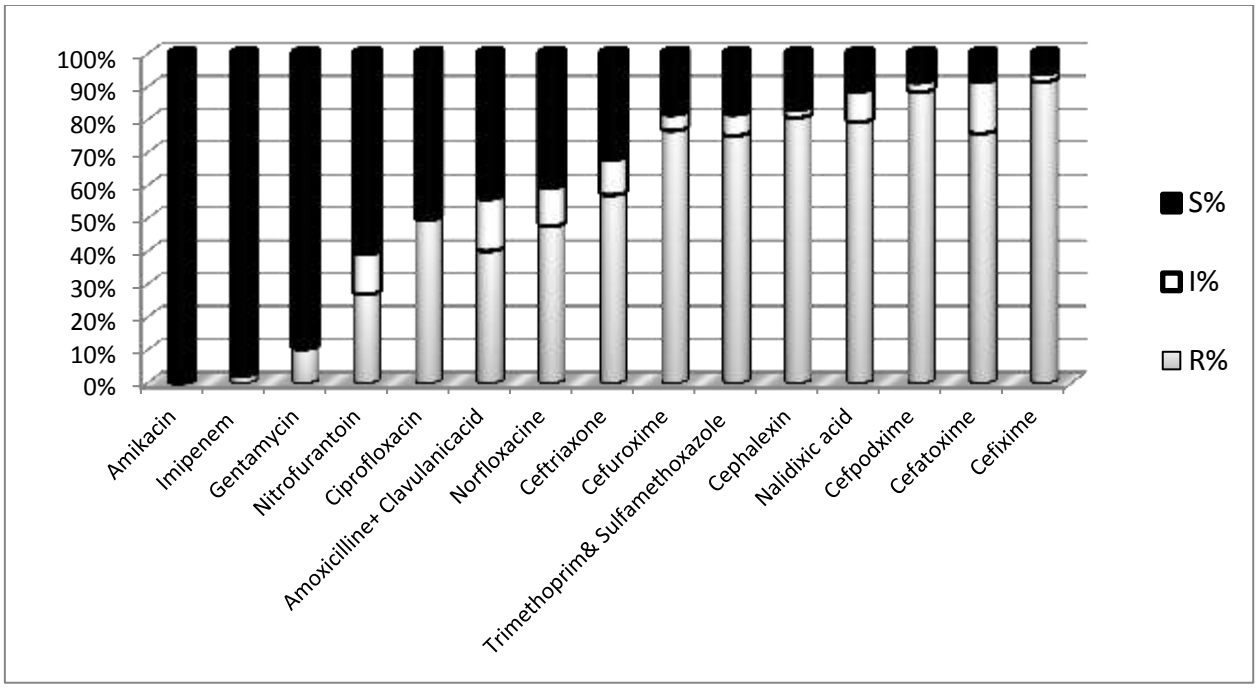

Figure 1: Antibiotic susceptibility results of 185 urine samples from Syrian IUT patients. S: susceptible, I: intermediate, R: resistant.

A high rate of resistance (≥ 20%) was observed among the isolated urine bacteria to twelve antibiotics (80%). Only three antibiotics had a rate of resistance below 20% (20%). These results are consistent with several studies on uropathogen resistance, which have shown high rates of resistance and multiple antibiotic resistance. The susceptibility results of bacterial isolates from Syrian UTI patients demonstrated a high prevalence of multidrug resistance. Only two bacterial isolates were resistant to one antibiotic (1%), while 99% of bacterial isolates were resistant to at least two antibiotics.

Uropathogens Type

Figure 2 shows a comparison of antibiotic resistance rates between E. coli and Klebsiella isolated from female UTI patients. The resistance rates to Cephalexin, Cefixime, Cefpodoxime, Nalidixic acid, Cefotaxime, Trimethoprim-Sulfamethoxazole, Cefuroxime, Ceftriaxone, Ciprofloxacin, Nitrofurantoin, Gentamicin, and Amikacin were approximately similar for E. coli and Klebsiella. E. coli urine isolates were found to be more resistant to Norfloxacin and Imipenem than Klebsiella, while Klebsiella urine isolates were more resistant to Amoxicillin-Clavulanic acid than E. coli.

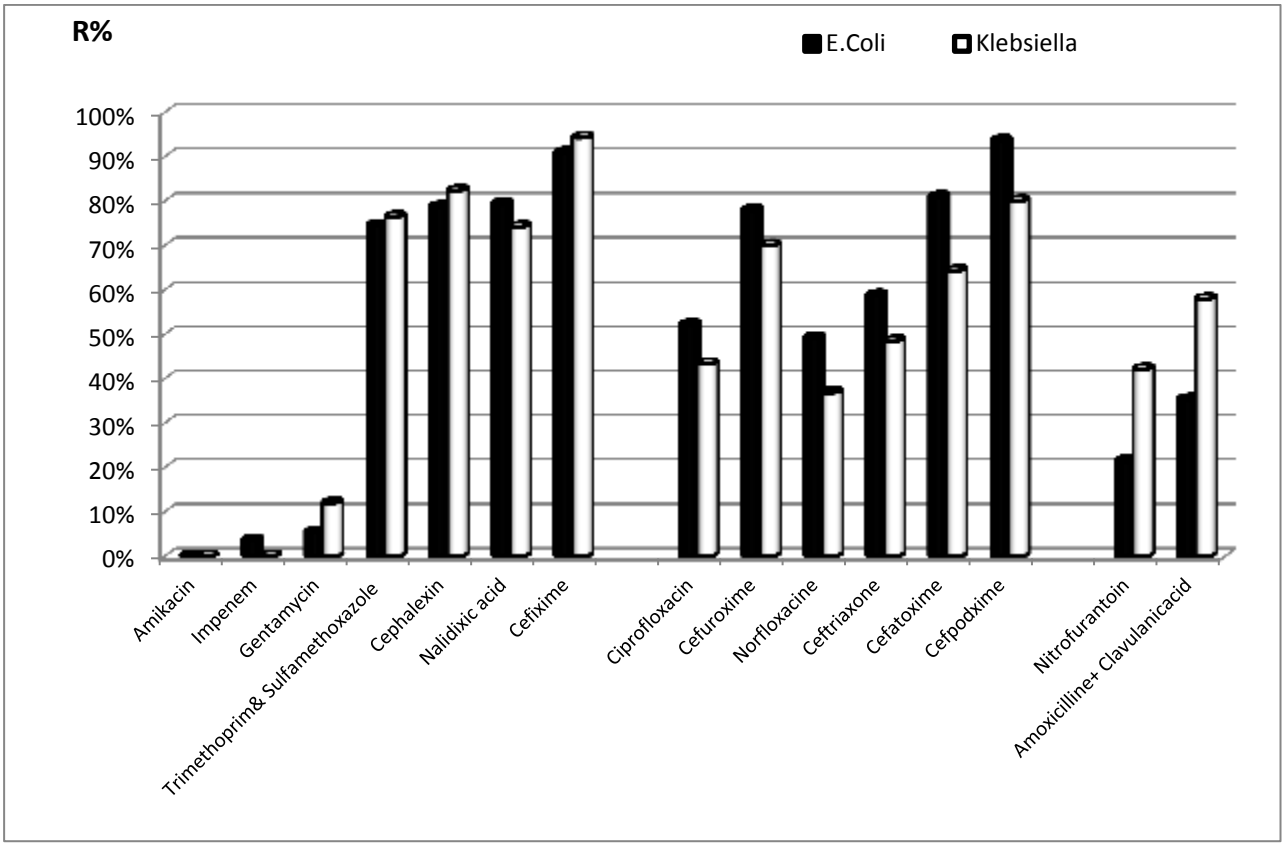

Figure2: resistance rate of *E. Coli* and *Klebsiella* urine isolates to studied antibiotics.

Patient age:

It was expected that the resistance rates would increase with female age. The effects of age on antibiotic resistance rates were assessed by comparing the susceptibility test results among urine isolates collected from pediatric patients (0 to 18 years of age) and adult patients (above 19 years of age).

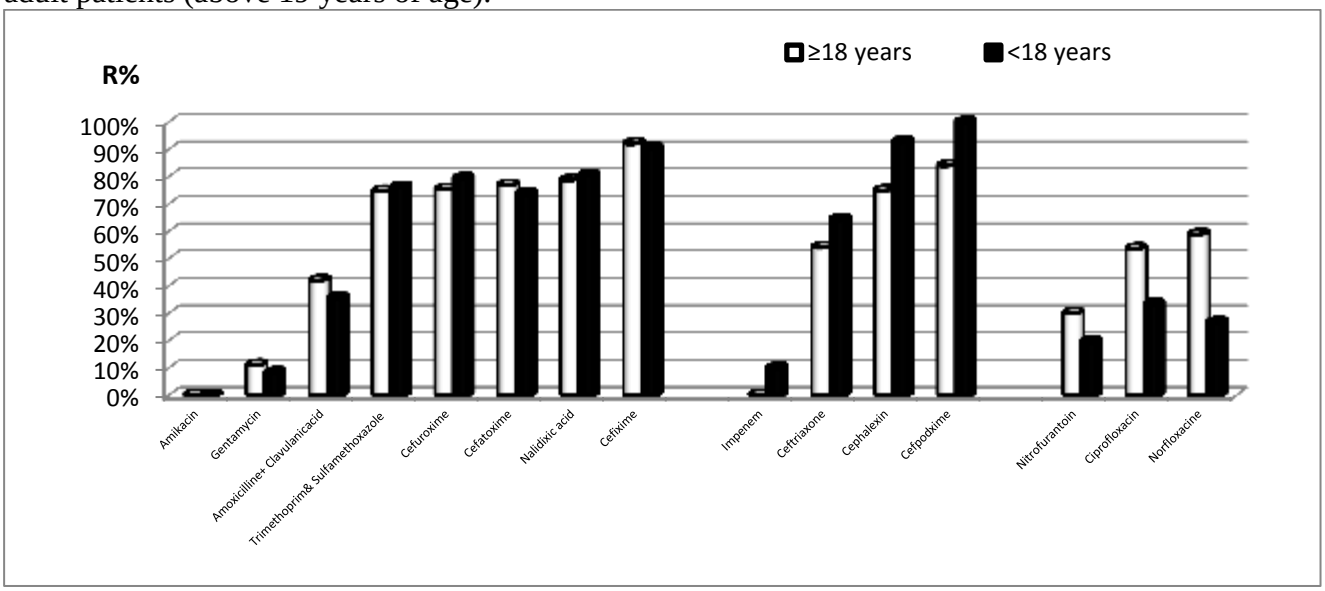

Figure3: comparison of resistance rate of urine isolates to studied antibiotics between two age groups (1: ≥18 years, <18nyears)

Figure 3 demonstrates a comparison of uropathogen resistance rates to the studied antibiotics with age, showing different trends with age. Similar resistance rates for the three age groups were observed for Amikacin, Trimethoprim-Sulfamethoxazole, Cephalexin, and Cefixime. Resistance rates to Nitrofurantoin, Ciprofloxacin, and Norfloxacin increased with female age. Urine bacteria isolated from UTI females between 19 to 65 years of age showed lower resistance rates than those obtained for females older or younger to Ceftriaxone, Nalidixic acid, Cefpodoxime, Cefuroxime, and Amoxicillin-Clavulanic acid. For Gentamicin, urine bacteria isolated from UTI females between 19 to 65 years of age had higher resistance rates compared to younger and older females. Only a few urine bacteria isolated from pediatric UTI females were resistant to Imipenem.

Patient Gender:

Figure 4 presents resistance rate of uropathogens to studied antibiotics taking in consideration gender differences. Similar resistance rates both in females and male urine samples were observed for Amikacin, Gentamycin, Norfloxacines, and Cefatoxine. Urine bacteria isolated from UTI females showed lower resistance percentages compared to males for Nitrofurantoin, Cefuroxime, Cefexime and Amoxicillin-Clavulanic acid. On the other hand, resistance percentages for Trimethoprim-Sulfamethoxazole, Nalidixic acid, Cefpodxime, Ceftriaxones, and mainly Cephalexin were higher in female compared to male samples.

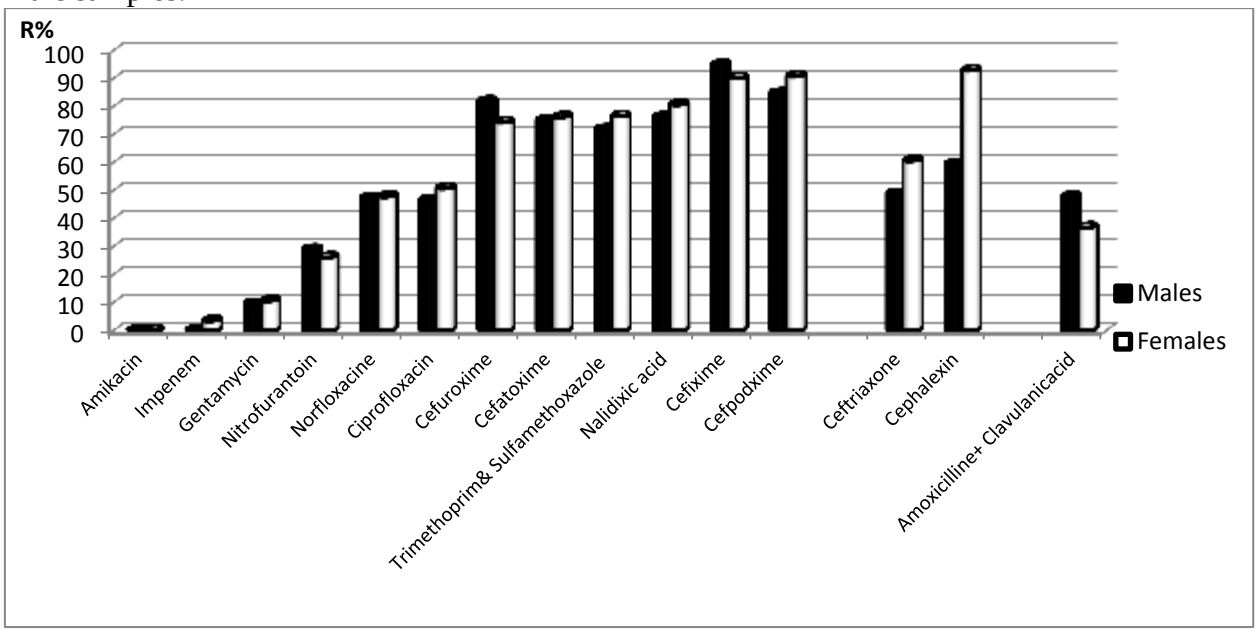

Figure 4: comparison of resistance rate of urine isolates to studied antibiotics between males and females.

Discussion:

The present study aimed to investigate the prevalence and antimicrobial susceptibility of uropathogens among Syrian patients with UTIs. A total of 185 urine samples were collected from August 2022 to June 2023 from female patients of different ages[18,19]. The samples were divided into two groups, i.e., pediatric patients (0 to 18 years of age) and adult patients (above 19 years of age). Among the studied UTI patients, the percentage of adult patients was higher (70%) than pediatric patients (30%). The most common uropathogen identified was Escherichia coli (68%), followed by Klebsiella

pneumoniae (24%) and other bacteria such as Enterobacter and beta-hemolytic streptococcus (8%).

The susceptibility of the isolated urine bacteria was tested against fifteen antibacterial drugs, including Amikacin, Gentamycin, Nitrofurantoin, Ceftriaxone, Ciprofloxacin, Imipenem, Nalidixic acid, Norfloxacin, Cefpodoxime, Cefuroxime, Cephalexin, Cefixime, Amoxicillin-Clavulanic acid, Trimethoprim-Sulfamethoxazole, and Cefotaxime. Figure 1 showed that all urine bacterial isolates were highly sensitive to Amikacin, Imipenem, and Gentamicin, while the percentage of sensitivity for urine bacterial isolates was low for Ceftriaxone, Cefuroxime, Trimethoprim-Sulfamethoxazole, Cephalexin, Nalidixic acid, Cefotaxime, Cefpodoxime, and Cefixime. A high rate of resistance (≥ 20%) was observed among the isolated urine bacteria to twelve antibiotics (80%). Only three antibiotics had a rate of resistance below 20% (20%), indicating a high prevalence of multidrug resistance among the uropathogens. Figure 2 showed a comparison of antibiotic resistance rates between E. coli and Klebsiella isolated from female UTI patients. The resistance ratesto most antibiotics were approximately similar for E. coli and Klebsiella. However, E. coli urine isolates were found to be more resistant to Norfloxacin and Imipenem than Klebsiella, while Klebsiella urine isolates were more resistant to Amoxicillin-Clavulanic acid than E. coli[20,21].

The effects of age on antibiotic resistance rates were assessed by comparing the susceptibility test results among urine isolates collected from pediatric patients and adult patients. Figure 3 demonstrated different trends with age. Similar resistance rates for the three age groups were observed for Amikacin, Trimethoprim-Sulfamethoxazole, Cephalexin, and Cefixime. Resistance rates to Nitrofurantoin, Ciprofloxacin, and Norfloxacin increased with female age. Urine bacteria isolated from UTI females between 19 to 65 years of age showed lower resistance rates than those obtained for females older or younger to Ceftriaxone, Nalidixic acid, Cefpodoxime, Cefuroxime, and Amoxicillin-Clavulanic acid. For Gentamicin, urine bacteria isolated from UTI females between 19 to 65 years of age had higher resistance rates compared to younger and older females. Only a few urine bacteria isolated from pediatric UTI femaleswere resistant to Imipenem. These findings suggest that age is a significant factor in the development of antibiotic resistance among uropathogens, which should be considered when selecting appropriate antibiotics for UTI treatment.

Conclussion:

In conclusion, this study aimed to investigate the prevalence and antimicrobial susceptibility of uropathogens among Syrian patients with UTIs. The results revealed that Escherichia coli was the most common uropathogen responsible for UTIs, followed by Klebsiella pneumoniae and other bacteria. The isolated urine bacteria showed high rates of resistance and multidrug resistance to several antibiotics, indicating the importance of careful selection of appropriate antibiotics for UTI treatment. The study also demonstrated that age is a significant factor in the development of antibiotic resistance among uropathogens, with resistance rates increasing with female age for some antibiotics. These findings highlight the need for continued surveillance and monitoring of antibiotic resistance patterns among uropathogens to inform appropriate treatment strategies.

References:

1. Kraemer, M. U., Yang, C. H., Gutierrez, B., Wu, C. H., Klein, B., Pigott, D. M., ... & Scarpino, S. V. (2020). The effect of human mobility and control measures on the COVID-19 epidemic in China. Science, 368(6490), 493-497.
2. Zhang, M., Xiao, J., Deng, A., Zhang, Y., Zhuang, Y., Hu, T., ... & Li, Y. (2021). Transmission dynamics of an outbreak of the COVID-19 Delta variant B. 1.617. 2—Guangdong Province, China, May–June 2021. China CDC weekly, 3(27), 584.
3. Vasudevan, R. (2014). Biofilms: microbial cities of scientific significance. J Microbiol Exp, 1(3), 00014.
4. Shukla, P. S., Mantin, E. G., Adil, M., Bajpai, S., Critchley, A. T., & Prithiviraj, B. (2019). Ascophyllum nodosum-based biostimulants: Sustainable applications in agriculture for the stimulation of plant growth, stress tolerance, and disease management. Frontiers in plant science, 10, 462648.
5. Schwaber, M. J., Navon-Venezia, S., Schwartz, D., & Carmeli, Y. (2005). High levels of antimicrobial coresistance among extended-spectrum-β-lactamase-producing Enterobacteriaceae. Antimicrobial agents and chemotherapy, 49(5), 2137-2139.
6. Morosini, M. I., García-Castillo, M., Coque, T. M., Valverde, A., Novais, A., Loza, E., ... & Cantón, R. (2006). Antibiotic coresistance in extended-spectrum-β-lactamase-producing Enterobacteriaceae and in vitro activity of tigecycline. Antimicrobial agents and chemotherapy, 50(8), 2695-2699.
7. Astal, Z., El-Manama, A., & Sharif, F. A. (2002). Antibiotic resistance of bacteria associated with community-acquired urinary tract infections in the southern area of the Gaza Strip. Journal of chemotherapy, 14(3), 259-264.
8. Flores-Mireles, A. L., Walker, J. N., Caparon, M., & Hultgren, S. J. (2015). Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nature reviews microbiology, 13(5), 269-284.
9. Colvin, M. T., Silvers, R., Ni, Q. Z., Can, T. V., Sergeyev, I., Rosay, M., ... & Griffin, R. G. (2016). Atomic resolution structure of monomorphic Aβ42 amyloid fibrils. Journal of the American Chemical Society, 138(30), 9663-9674.

10. Sireesh, D., Ganesh, M. R., Dhamodharan, U., Sakthivadivel, M., Sivasubramanian, S., Gunasekaran, P., & Ramkumar, K. M. (2017). Role of pterostilbene in attenuating immune mediated devastation of pancreatic beta cells via Nrf2 signaling cascade. The Journal of nutritional biochemistry, 44, 11-21.
11. Sahoo, S. N., & Sreeja, P. (2017). Development of flood inundation maps and quantification of flood risk in an urban catchment of Brahmaputra River. ASCE-ASME Journal of Risk and Uncertainty in Engineering Systems, Part A: Civil Engineering, 3(1), A4015001.
12. Joshi, N., Hayasaka, T., Liu, Y., Liu, H., Oliveira, O. N., & Lin, L. (2018). A review on chemiresistive room temperature gas sensors based on metal oxide nanostructures, graphene and 2D transition metal dichalcogenides. Microchimica Acta, 185, 1-16.
13. Sindhwani, S., Syed, A. M., Ngai, J., Kingston, B. R., Maiorino, L., Rothschild, J., ... & Chan, W. C. (2020). The entry of nanoparticles into solid tumours. Nature materials, 19(5), 566-575.
14. Aljanaby, A. A. J., & Alhasnawi, H. M. R. J. (2017). Research article phenotypic and molecular characterization of multidrug resistant Klebsiella pneumoniae isolated from different clinical sources in Al-Najaf Province-Iraq. Pak. J. Biol. Sci, 20(5), 217-232.

15. Rana, S., & Sirwar, S. B. (2015). Prevalence and Antibiogram of Extended Spectrum β-Lactamase Producing Klebsiella pneumoniae and Proteus mirabilis in UTI. Research Journal of Pharmacy and Technology, 8(11), 1465-1468.
16. Abbood A, Malek Z, Al-Homsh Y, Thallaj N. In vitro Study for Antibiotic resistance of bacteria causing Urinary Tract Infection from Syrian adults. Research Journal of Pharmacy and Technology. 2022;15(10):4727-2. doi: 10.52711/0974-360X.2022.00794.
17. Abbood A, Malek Z, Thallaj N. Antibiotic resistance of urinary tract pathogens in Syrian children. Research Journal of Pharmacy and Technology. 2022;15(11):4935-9. doi: 10.52711/0974-360X.2022.00829.
18. A.Abbood, Z.Malek, N.Thallaj. 2022 65, 6, 302-312. Xi'an ShiyouDaxueXuebao (ZiranKexue Ban)/ Journal of Xi'an Shiyou University, Natural Sciences Edition.
19. Negri, M., Lima, B. M., Woloszynek, R. D. S. B. R., Molina, R. A. S., Germano, C. M. R., Melo, D. G., ... & Avó, L. R. D. S. D. (2024). Prevalence and antimicrobial resistance profile of pathogens isolated from patients with urine tract infections admitted to a university hospital in a medium-sized Brazilian city. Revista do Instituto de Medicina Tropical de São Paulo, 66, e3.
20. Sado, K., Keenan, K., Manataki, A., Kesby, M., Mushi, M. F., Mshana, S. E., ... & HATUA Consortium. (2024). Treatment seeking behaviours, antibiotic use and relationships to multi-drug resistance: A study of urinary tract infection patients in Kenya, Tanzania and Uganda. PLOS Global Public Health, 4(2), e0002709.