CHANGING PATTERNS IN SENSITIVITY OF BACTERIAL UROPATHOGENS TO ANTIBIOTICS BETWEEN 2018 AND 2023

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Abstract: This study investigates the evolving antibiotic sensitivity patterns of bacterial uropathogens over a six-year period from 2018 to 2023. With increasing antibiotic resistance posing a significant challenge to effective urinary tract infection (UTI) management, the research analyzes susceptibility data from clinical isolates to identify trends in resistance and sensitivity. Key bacterial species responsible for UTIs, including Escherichia coli, Klebsiella pneumoniae, and Enterococcus faecalis, were evaluated against commonly prescribed antibiotics. The findings reveal shifts in resistance profiles, highlighting a growing resistance to traditionally used antibiotics such as fluoroquinolones and cephalosporins, while some newer agents show retained efficacy. This study underscores the urgent need for continuous surveillance, updated antibiotic stewardship programs, and tailored treatment guidelines to optimize patient outcomes and combat the rise of multidrug-resistant uropathogens.

Key words: Urinary tract infection, sensitivity, resistance, bacterial uropathogen, Uropathogens, Antibiotic Sensitivity.

ИЗМЕНЕНИЕ ЗАКОНОМЕРНОСТЕЙ ЧУВСТВИТЕЛЬНОСТИ БАКТЕРИАЛЬНЫХ УРОПАТОГЕНОВ К АНТИБИОТИКАМ В ПЕРИОД 2018–2023 ГОДОВ

Аннотация: В этом исследовании изучаются закономерности изменения чувствительности к антибиотикам бактериальных уропатогенов за шестилетний период с 2018 по 2023 год. Поскольку растущая резистентность к антибиотикам представляет собой значительную проблему для эффективного лечения инфекций мочевыводящих путей (ИМП), в исследовании анализируются данные о восприимчивости клинических

изолятов для выявления тенденций в резистентности и чувствительности. Основные виды бактерий, ответственные за ИМП, включая Escherichia coli, Klebsiella pneumoniae и Enterococcus faecalis, были оценены по сравнению с обычно назначаемыми антибиотиками. Результаты показывают изменения в профилях резистентности, подчеркивая растущую резистентность к традиционно используемым антибиотикам, таким как фторхинолоны и цефалоспорины, в то время как некоторые новые агенты демонстрируют сохраненную эффективность. В этом исследовании подчеркивается настоятельная необходимость постоянного наблюдения, обновленных программ управления антибиотиками и индивидуальных рекомендаций по лечению для оптимизации результатов лечения пациентов и борьбы с ростом уропатогенов с множественной лекарственной устойчивостью.

Ключевые слова: Инфекция мочевыводящих путей, чувствительность, резистентность, бактериальный уропатоген, уропатогены, чувствительность к антибиотикам.

Introduction

Urinary tract infections (UTIs) are one of the most common types of bacterial infections in humans, occurring both in the community and in healthcare settings. UTI refers to a wide range of clinical conditions, from the asymptomatic presence of bacteria in the urine to severe kidney infection with subsequent sepsis.[1] Females are more prone to UTIs than males, a phenomenon explained by their short urethra and its anatomical proximity to the anal orifice.[2,3] Uropathogens are simple to identify as they mainly come from colonic flora,[4] and this serves as a rationale for the empirical treatment of community acquired UTI (CA-UTI).[2,5] Empirical treatment, on the other hand, limits the ability to monitor antibiotic response and predisposes uropathogens that cause UTI to resistance.[5,6] Despite their use as practical methods for efficient resource use, empirical management plans must be regularly updated to account for shifting pathogen susceptibility patterns.[6] This is

particularly true for developing nations, where the lack of resources for routine antibiotic sensitivity test compounds an additional challenge.[6]

In recent years, the resistance of uropathogens to previously effective antibiotics has become a global phenomenon.[7–9] Antimicrobial resistance (AMR) is currently estimated to account for more than 700,000 deaths per year worldwide.[10] If no appropriate measures are taken to halt its progress, it is projected to cost approximately 10 million lives and about US$100 trillion per year by 2050.[10] In contrast to other health issues, Anti-microbial Resistance (AMR) is a problem that concerns every country, irrespective of its level of income and development. According to the WHO report from 2014, Africa and South-East Asia are the regions with no established AMR surveillance systems.[11] The lack of quality data is challenging, resulting in inadequate treatment guidelines for the local situation. The gap in public health capacity is also an issue given the rapidly evolving resistance mechanisms of the pathogens and the emergence of multidrug-resistant bacteria that can only be detected through systematic screening in quality-assured microbiology laboratories.[12,13] Given the widespread irrational use of antibiotics in Africa, the situation is dire[9,11] as compared to developed nations.

To design suitable interventions, it is important to understand the status of AMR and identify rollout gaps. The most recent version of the national Ethiopian treatment guideline recommends using Trimethoprim/Sulfamethoxazole (TMP-SMX) and Norfloxacin for the empirical treatment of CA-UTI in Ethiopia, one of the second-most populous regions of Africa.[14] However, we believe that there might be significant antibiotic resistance to the recommended treatments, and as a result, the likelihood of treatment failure is rising with the continued empirical use of these medications. As such, the study aimed to assess antibiotic resistance to both the suggested treatments and other drugs, as well as to identify patterns of resistance to a wide range of potentially helpful alternatives for the treatment of UTIs in Uromed Clinic, Ferghana, Uzbekistan.

Methodology

This study was conducted at the Uromed Clinic Ferghana/Uzbekistan. Medical records urologic patients who diagnosed of UTI (inpatient and outpatient) were evaluated from 2018 to 2023 years, and patients who had positive urine cul ture in association with pyuria were selected for research. Clinical diagnosis was based on the presence of one or more of followings: fever, flank pain, dysuria, frequency, urgency and supra- pubic pain. Pyuria was defined as the presence of more than seven leukocytes in high power filed of centrifuged urine. Positive urine culture was defined as more than 10^5 colony forming units (CFU) of a single organism per milliliter of urine. Urine specimens were obtained by midstream (morning urine) collection. Suprapubic sampling was carried out in selected patients. Blood agar was used for urine culture. Sensitivity/resistance of isolated microorganisms to commonly used antibiotics was detected by disc diffusion method. Exclusion criteria were: patients without pyuria, asymptomatic patients and positive cultures with less than 10^5 CFU/ml or multiorganism growth. Also patients with insufficient data and repeat isolates from the same patient were excluded. Data from each patient including sex, age, clinical symptoms, and results of urine analysis, urine culture and antibiogram were collected in organized form.

Results

From 2018 to 2020, 400 patients and from 2021 to 2023, 350 patients who fulfilled the inclusion criteria were studied. Demographic features of patients have been demonstrated in Table-I. E.Coli, Staphylococcus epidermidis, enterobacter, were the most common isolated germs in both periods of study (Table-II). The in vitro sensitivity of E.Coli and Staphylococcus epidermidis to antibiotics has been shown in (Table-III&IV). In study of 2018 and 2020: Among the oral agents, levofloxacin and azithromycin, and among the parenteral agents, ceftriaxone had the highest activity against E.Coli.

Period of study	No. of patients	No. of males (%)	No. of females (%)

2018-2020	400	145 (36.25%)	255 (63.75%)
2021-2023	350	120 (34.28%)	230 (65.71%)

Microorganism	№ (%) in 2018-2020	№ (%) in 2021-2023
E.Colli	169 (42.25%)	160 (45.71%)
Staphylococcus epidermidis	105 (26.25%)	171(48.85%)
Enterobacter	36 (9%)	10 (2.85%)
Candida alba	20 (5%)	5 (1.42%)
Others	61 (15.25%)	4 (1.14%)
Total	400	350

The highest sensitivity of Staphylococcus epidermidis was to levofloxacin, ceftriaxone, azithromycin in a descending order. (Table-IV). The activity of levofloxacin, azithromycin, ceftriaxone, against E. coli has de- creased significantly over six years ($P<0.05$). Also the activity of levofloxacin, ceftriaxone, azithromycin against Staphylococcus epidermidis has decreased in comparison with results of six years ago ($P<0.05$). There was not any significant change in susceptibility of E. coli and Staphylococcus epidermidis to other antibiotics in two periods of study. In study of 2018-2020, the sensitivity of enterobacter was 78.5% to gentamicin, 71.4% to ceftazidime, 57.1% to ciprofloxacin and ceftriaxone, 50% to amikacin and nitrofurantoin, 42.8% to nalidixic acid and 35.7% to co-trimoxazol. The sensitivity of candida alba was 100% to ciprofloxacin and ceftazidim, 81.8% to gentamicin and 63.6% to amicacin. All other antibiotics were totally inactive against candida alba. There was not any significant difference in antibacterial sensitivity of enterobacter and candida alba in two periods of study ($P>0.05$).

Discussion

Escherichia-coli is the most common cause of UTI and accounts for 75-90% of UTIs.[6,7] However its relative frequency varies in different areas. In studies carried out in Canada, Mexico, Pakistan and India E. coli accounted for 57.7%-

69.9% and Staphylococcus epidermidis for 12.4%-29% of UTIs,[8-11] that is similar to our results. In empiric treatment of acute febrile UTI, suggestive of pyelonephritis, broad spectrum antibiotics such as ceftriaxone or a combination of ampicillin with an aminoglycoside such as gentamicin is conventionally recommended.[6,12] However in some studies from Iran,[4,13] Mexico[9] and Sudan,[14] microbial resistance to ampicillin is high and varies from 75% to 89.3%. In present study, resistance to ampicillin is very high (91.8%). So adminstration of ampicillin in empiric treatment of UTI is not reasonable in our center. Most studies show a high sensitivity of E.coli to gentamicin.[15] In the study of Goldstein et al in France, the susceptibility of E.coli to gentamicin was 98.4%.[16] In our study the susceptibility of E.coli is 69.9% to gentamicin and 84.4% to amikacin which is lower than other studies. Also present study showed that the activity of ceftriaxone against E. coli and Staphylococcus epidermidis and activity of aminoglycosides against Staphylococcus epidermidis has significantly decreased over five years. Decreasing trend in activity of aminoglycosides and third generation cephalosporines against uropathogens raises a great concern regarding the empiric treatment of pyelonephritis, in our institution.

Among oral antibiotics for ambulatory management of uncomplicated lower UTI, cotrimoxazol was a drug of choice for a long time. During the past decades resistance of E. coli to cotrimoxazol increased from 0-5% be- fore 1990 to 9-15% in 1999 in Western countries.[17] In recent years resistance of E. coli to cotrimoxazole has increased and varies from 21% to 76.7% in different studies.[8-10,13-15,18-22] In our study, resistance of E. coli to cotrimoxazol (82.2%) is higher in comparison with literature that may be related to inappropriate prescription of cotrimoxazol in upper respiratory infections in our country. From other oral agents fluoroquinolones (FQs) such as ciprofloxacin have the highest activity against E.Coli in most studies.[14,16,18-20] So in the past few years use of cotrimoxazol has

decreased whereas use of FQs has increased dramatically in adults.[23] Guneysel et al observed that FQs were the most prescribed antibiotics for UTI of adults in Turkey.[20] The activity of ciprofloxacin against E.coli has been reported up to 93.3% in children[4] and is 81.5% in our study. However, the safety of ciprofloxacin in children is under study because of potential cartilage damage that occurred in research with immature animal.

Conclusion

This study has showed a decreasing suscep tibility of E. coli and Staphylococcus epidermidis to some antibiotics over a five years period. If this trend continues, the antimicrobial drugs are likely to become less effective not only for treating of UTI, but also for treating of other life threatening infections. However, it should be noted that our clinic is a referral center for most complicated UTIs. Further community based studies in general hospitals and outpatient settings are required to determine the resistance pattern of uropathogens in uncomplicated UTIs.

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