ORIGINAL ARTICLE

INVESTIGATION OF ANTIBIOTIC RESISTANCE RATES OF BACTERIA CAUSING URINARY SYSTEM INFECTION

Üriner Sistem Enfeksiyon Etkeni Bakterilerin Antibiyotik Direnç Oranlarının Araştırılması

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ABSTRACT

Objective: Urinary tract infection (UTI) is a prevalent health concern globally. The objective of this study was to evaluate the frequencies of pathogens associated with UTI and their antimicrobial susceptibility patterns, as well as extended-spectrum beta-lactamase (ESBL) rates.

Material and Methods: Urine culture results between January 2023 and December 2023 were examined retrospectively. Additionally, variables such as age, sex, and medical department were documented. The study included patients aged 18 years or above with pathogenic bacterial growth in their urine cultures. The identification of bacteria and their antibiotic susceptibility was conducted using conventional methods or the VITEK2-Compact system.

Results: Of 3135 urine samples considered to be causative agents were evaluated. 2495 Escherichia coli, 404 Klebsiella spp., 117 Proteus mirabilis, 57 Pseudomonas spp., 19 Acinetobacter spp., and 43 other enterobacterales members were detected. ESBL positivity rates were found to be for E. coli 14.9% and for Klebsiella spp. 23.2%. Resistance rates of hospital-acquired infection agents were found to be significantly higher than community-acquired. More than 90% susceptibility to carbapenems and aminoglycosides has been detected.

Conclusion: It is beneficial to be aware of the evolution of antibiotic resistance over time, particularly when embarking on empirical therapy. The elevated level of quinolone resistance in hospital-acquired infections can be attributed to its utilisation for a multitude of indications, including pneumonia, gastroenteritis, and urinary tract infections. Our findings indicate that ciprofloxacin, trimethoprim-sulfamethoxazole, and ampicillin are unsuitable for the empirical treatment of UTIs, while nitrofurantoin and fosfomycin represent rational options. We believe that these data will shed light on empirical treatments in our hospital.

Keywords: *Antibiotics; Escherichia Coli; Urinary Tract İnfections; Esbl; Klebsiella Spp.*

ÖZET

Amaç: İdrar yolu enfeksiyonu (İYE) yaygın küresel bir sağlık sorunudur. Bu çalışmada amacımız, hastane kökenli ve toplum kökenli üropatojenlerin sıklıklarını ve antimikrobiyal duyarlılık paternlerinin yanı sıra genişlemiş spektrumlu beta-laktamaz (GSBL) oranlarını araştırmaktır.

Gereç ve Yöntemler: Ocak 2023 ve Aralık 2023 tarihleri arasındaki hastalara ait idrar kültür sonuçları retrospektif olarak incelenmiştir. Yaş, cinsiyet ve örneğin gönderildiği bölüm araştırılmıştır. Çalışmaya, idrar kültürlerinde üreyen ve etken olarak değerlendirilen 18 yaş ve üzeri hastalara ait kültür sonuçları dahil edilmiştir. Bakterilerin tanımlanması ve antibiyotik duyarlılıkları geleneksel yöntemler ve VITEK2-Compact sistemi kullanılarak gerçekleştirilmiştir.

Bulgular: Etken kabul edilen 3135 Gram negatif üropatojen irdelenmiştir. 2495 Escherichia coli, 404 Klebsiella spp., 117 Proteus mirabilis, 57 Pseudomonas spp., 19 Acinetobacter spp. ve 43 diğer enterobacterales üyeleri tespit edilmiştir. GSBL pozitiflik oranları E. coli için %14,9 ve Klebsiella spp. için %23,2 olarak bulunmuştur. Hastane kökenli enfeksiyon etkenlerinin direnç oranları toplum kökenlilere göre anlamlı derecede yüksek bulunmuştur. Karbapenemlere ve aminoglikozidlere karşı %90'dan fazla duyarlılık tespit edilmiştir.

Sonuç: Hastane kaynaklı enfeksiyonlarda yüksek kinolon direnci seviyesi, pnömoni, gastroenterit ve idrar yolu enfeksiyonları dahil olmak üzere çok sayıda endikasyonda kullanılmasına bağlanabilir. Bulgularımız, siprofloksasin, trimetoprim-sülfametoksazol ve ampisilinin İYE'lerin ampirik tedavisi için uygun olmadığını, nitrofurantoin ve fosfomisinin ise rasyonel seçenekler olduğunu göstermektedir. Bu verilerin hastanemizdeki İYE ampirik tedavilerine ışık tutacağına inanıyoruz.

Anahtar Kelimeler: *Antibiyotikler; Escherichia Coli; İdrar Yolu Enfeksiyonları; Gsbl; Klebsiella Spp.*

INTRODUCTION

One of the most common bacterial infections is urinary tract infection (UTI). There are an estimated about 200 million cases documented globally each year (1). In over 95% of cases of urinary tract infection, a monobacterial infection is observed, with a higher prevalence in females except during the first three months of life (2). The presentation of UTI can range from a relatively mild form, such as cystitis, to a more severe and potentially life-threatening condition like urosepsis (3). Additionally, the spectrum of pathogens responsible for UTI can vary significantly, particularly depending on geographical location. It is of paramount importance to select an appropriate antibiotic that is efficacious against the causative organism to treat UTI (4).

Developing bacterial resistance mechanisms also presents a challenge to the treatment of these infections. One of the crucial benchmarks in the stewardship of antimicrobial resistance is the implementation of a treatment policy in accordance with the findings of antibiotic susceptibility tests (5). As a consequence, inadequate treatment is delivered, the requirement for empirical treatment modifications arises and hospitalisation periods are extended. Furthermore, the necessity for empirical treatments increases costs, while morbidity and mortality rates also rise (6).

While urinary tract infections (UTIs) are typically caused by a single bacterium, other common and isolated bacteria may also be involved. These include E. coli, Klebsiella spp., Pseudomonas spp., Proteus spp., Enterobacter spp., enterococci and staphylococci (7).

The inappropriate and/or improper utilisation of antibiotics renders the treatment of UTIs an increasingly challenging endeavour (8). Frequently, antibiotics are initiated empirically, yet this approach may not be as effective as previously thought. The primary challenge in achieving successful empiric UTI therapy is the emergence of antibiotic-resistant bacteria. This resistance can be intrinsic, acquired or clinical. The prevalence of antibiotic-resistant bacteria is likely to be exacerbated by factors such as poor patient compliance and the utilisation of an inappropriate diagnostic approach. In order to select an appropriate antibiotic regimen, it is essential to implement a resistance surveillance programme. The European urology guideline states that antibiotics with resistance above certain rates are not suitable for use in empirical treatment (9,10).

There are limited number of studies on antibiotic susceptibilities of urinary tract infectious agents in the region where our hospital is located. The aim of this study was to determine the distribution of Gram-negative microorganisms, causative bacteria and antibiotic resistance rates of community-acquired (CA) and hospital-acquired (HA) UTIs by retrospectively analysing urine culture results.

MATERIAL AND METHODS

The study was conducted in the Ankara province, which is a metropolitan city located in the capital of Turkey. The hospital is a tertiary-level training and research facility with a bed capacity of 625. It serves a population of approximately 1 million, with an annual average of 250,000 emergency admissions. Urine specimens sent to the microbiology laboratory of Sincan Training and Research Hospital between January 2023 and December 2023 from a range of wards, out patient clinics and intensive care units with evidence of pathogenic bacteria growth were included in the study. The culture results were analyse using the laboratory information system. The inclusion criteria were as follows: the subject must have been at least 18 years of age, the urine cultures must have been performed in the laboratory, and there must have been pathogenic growth in the culture results. Patients with culture requests but no growth, and those with growth but for whom typing could not be performed for example, due to the presence of fungal or other anaerobic bacterial growths (anaerobic culture is not conducted) or polymicrobial growths—were excluded from the study. In instances of recurrent growths, the result of the initial sample was taken into consideration. The antibiotic susceptibility results of the microorganisms were categorised according to gender, age, outpatient and inpatient status. The susceptibility rates of the antibiotics (amikacin, ampicillin, amoxicillin/clavulanicacid, ceftriaxone, ceftazidime, ciprofloxacin, fosfomycin, gentamicin, meropenem, ertapenem, nitrofurantoin, piperacillin/tazobactam, trimethoprim/sulfamethoxazole) (Bioanalyse, Turkey) were recorded.

Developing in the community or occur within the first 48 hours of hospitalization are defined as community-acquired UTIs (11). A quantitative analysis of the urine samples was conducted on both blood agar and eosin methylene blue (EMB) agar media, employing a sterile inoculation loop. The samples were then incubated in an aerobic environment at 37°C for a duration of 24 hours. Samples with bacterial growth of 10^4cfu/ml and above; Identification of lower numbers of microorganisms thought to be causative and antibiotic susceptibility tests were performed, taking into account characteristics such as the number of breeding colonies, the number of species, the presence of leukocytes in the urine sample, and the clinical condition of the patient (12). Isolated bacteria Gram staining, catalase test, oxidase test, carbohydrate and citrate use. Bacterial typing and susceptibility testing were conducted using conventional disc diffusion and an automated VITEK 2 Compact system (bioMerieux, Marcy-l'Étoile, France). The results of the antibiotic susceptibility tests were evaluated in accordance with the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The production of extended-spectrum beta-lactamases (ESBL) was determined through the utilisation of a double disk synergy test and the Vitek2 automated system (13). The study was approved by Ankara Bilkent City Hospital (Decision no. - TABED 1-24-574). The study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments or similar ethical standards.

Statistical Analysis

The data were analysed statistically using IBM SPSS Statistics 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The data were expressed as numbers and percentages in accordance with the Fisher exact test. In the analysis of the results, the Fisher exact test and the chi-square test were employed, and values with a p-value of less than 0.05 were considered to be statistically significant.

RESULTS

In our study, 3,135 urine samples, determined to be the causative agent and sent to our laboratory from various outpatient clinics and services, and for which antibiotic susceptibility tests were performed, were evaluated. Of the total number of samples studied, 77.9% (2,442) were from female patients and 22.1% (693) were from male patients. The median age was found to be 43.1 ± 16.3 (range: 0–95) years. A total of 2,869 (91.5%) of the urinary tract infections were determined to be CA, while 266 (8.5%) were determined to be HA. A single bacterium was isolated in all samples. The distribution of the factors according to clinics and at the bacterial level is shown in Table 1. It has been demonstrated that there is a statistically significant increase in resistance to all antibiotics except meropenem, ertapenem, amikacin and gentamicin in HAIs compared to CAIs. Antibiotic susceptibility rates of Enterobacterales species in CA and HAIs are shown in Table 2. ESBL positivity rates were found to be 14.9% and 23.2% for E.coli and Klebsiella spp, respectively.

DISCUSSION

UTIs are among the top infections that occur both in the hospital and in the community (14). The importance of these infections is increasing due to high recurrence rates and increasing antibiotic resistance in

Table 1. Distribution of bacteria causing urinary system infections according to clinics and distribution of bacteria caused by CA-HA

Clinics	N	Bacteria	CA-UTI (N=2869)	HA-UTI (N=266)
Urology	1040	E.coli	2381(%82.9)	114
Gynecological Diseases	703	Klebsiella spp.	308(%10.7)	96
Pediatry	490	Proteus spp.	99(%3.4)	18
Internal Medicines	478	Pseudomonas spp.	32(%1.1)	25
Urgent	105	Acinetobacter spp.	13(%0.4)	6
ICU	122	Others enterobacterales	36(%1.2)	7
Others	197			

ICU:Intensive care units CA:Community acquired HA:Hospital acquired UTI:Urinary tract infection

Table 2. Antibiotic susceptibility rates of Enterobacterales species (%)

Antibiotics	CA Infection Susceptibility (%)	HA Infection Susceptibility (%)	Total Susceptibility (%)	p
Ampicillin	%34.1	%8.2	%31,5	<0.001
AMC	%57.1	%11.2	%52.5	<0.001
Ceftazidime	%74.2	%28.5	%69.6	<0.001
Ceftriaxone	%73.8	%25.8	%69	<0.001
Nitrofurantoin (for E.coli)	%98.4	%73.6	%95.9	<0.001
Fosfomycin (for E. coli)	%97.1	%14.3	%88.8	<0.001
Ciprofloxacin	%82	%36	%77.4	<0.001
Amikasin	%99.2	%74.3	%96.7	<0.001
Gentamicin	%94	%64.9	%91.8	<0.001
TMP-SXT	%74.1	%38.3	%70.5	<0.001
TZP	%61.9	%53.9	%61	<0.001
Meropenem	%99.4	%89.8	%98.4	<0.001
Ertapenem	%96.4	%86.4	%95.4	<0.001

AMC:Amoxicillin-clavulanate; TZP:Piperacillin-tazobactam; TMP-SXT:Trimethoprim-sulfamethoxazole

isolated bacteria (15). The gold standard method in the diagnosis of UTI is culture (16). Culture and antibiogram procedures complete at least two days, which leads to the application of empirical treatment. To ensure the appropriate selection of antibiotics for empirical treatment, it is essential that each region and each centre conducts regular monitoring of the agent distribution and antibiotic resistance status (17). The most common cause of CA and HA UTIs in all age groups is Gram-negative bacteria, and the most frequently isolated agent is E.coli (50-90%), followed by Klebsiella pneumoniae. In a study, four-year urinary system infection agents were analyzed and Enterobacterales species were detected in 73.7% of urine cultures with bacterial growth. The most frequently isolated agent was E. coli (55.6%), while the second most frequently isolated agent was identified as K. pneumoniae (14.2%) (18). Similarly, in our study, Enterobacterales species were isolated as the causative agent from the majority of the samples. Of these, 82.9% were E.coli and 10.7% were Klebsiella spp. While the rate of E. coli is decreasing in HAIs, the rate of Klebsiella spp. has increased.

In a study, CAIs were detected E. coli (58.2%), Klebsiella spp. (10.8%) and E. faecalis (6.7%); In HAI, E. coli (47%), E. faecalis (9.4%), P. aeruginosa (6.6%) were detected (19). When the distribution of bacteria causing UTIs was examined in other studies investigating the prevalence of HAIs, the first place was; E. coli and Enterococcus faecium (20,21).

In our study, the HAI agent ranking was made for Gram negatives, and results similar to the literature were found. This shows that although resistance rates may change over the years, there is no significant change in the bacterial species that cause HAIs.

In our study, general antibiotic resistance rates of Enterobacterales strains were found as ampicillin 31.5%, AMC 52.5%, ceftriaxone 69%, TMP-SXT 70.5%, ciprofloxacin 77.4%, aminoglycoside >90% and carbapenem >95%. E. coli, the most common causative agent of UTIs, was 3% for fosfomycin and 2% for nitrofrontain. In a study evaluating E. coli isolates grown in urine culture, these rates were found to be 4% for fosfomycin and 4% for nitrofurantoin, which is compatible with our study (22). In addition, in our study, it was found that antibiotic susceptibilities of Enterobacterales species were lower in HAIs compared to CAIs. The existence of susceptibility limit values for in uncomplicated urinary tract infections for fosfomycin should be taken into consideration when using it in empirical treatment.

In a study conducted with enteric bacteria grown in urine cultures, resistance to amikacin, gentamicin, and imipenem was not reported. In a study revealing antibiotic resistance rates in ESBL-positive Enterobacterales isolates, the resistance rate was found to be 0.3% for imipenem and 3.5% for amikacin (12,23). In our study, the antibiotics with the lowest resistance rates in Enterobacterales species were ertapenem (5%), meropenem (2%), amikacin (3%) and gentamicin (8%).

The results of our study indicate that the prevalence of antibiotic resistance among the bacteria commonly associated with UTIs is relatively high. A review of the literature reveals that studies have reported results that are consistent with our findings in the context of E. coli bacteria (5,7,12). In conclusion, there is overwhelming evidence that the implementation of antimicrobial stewardship programmes in our country, which have been in place for approximately 20 years, is of significant benefit and should be expanded. However, individual reports have indicated discrepancies in regional antibiotic susceptibility rates. It is recommended that clinicians consider both international guidelines and local antibiotic resistance rates, particularly when making decisions regarding the empirical treatment of urinary tract infections. There sults of our study indicate that ciprofloxacin, co-trimoxazole, and ampicillin are not recommended for the empirical treatment of UTIs. Conversely, there is evidence that indicates that nitrofurantoin and fosfomycin are effective pharmaceutical agents that warrant further consideration.

It appears that, in addition to the elevated resistance rates observed in relation to frequently prescribed drugs in outpatient settings, increased resistance rates have also been documented in relation to antibiotics such as piperacillin-tazobactam, carbapenem and aminoglycoside group antibiotics employed in inpatient settings (24,25). This illustrates the significance of adapting the course of treatment in accordance with the results of the culture test. Quinolone resistance rates in HA infectious agents were found to be significantly higher than CA ones (24-26). This is due to the use of quinolones for many reasons such as pneumonia, gastroenteritis, and urinary tract infections.

The increasing prevalence of extended-spectrum beta-lactamases (ESBLs) represents a further challenge in the management of urinary tractinfections (UTIs). A study conducted in our country revealed that ESBL positivity was 50.5% in HA UTIs caused by E. coli and 38.2% in CA UTIs (27). A review of the literature reveals considerable variation in the rates of resistance observed in different regions of the world. One such study, conducted at multiple centres in China, reported a 37.2% ESBL positivity rate, which is comparable to our own findings (28). The rising prevalence of ESBLs represents a significant concern in the management of UTIs. The discrepancy in ESBL rates has been linked to numerous factors (28). For instance, the inappropriate utilisation of antibiotics and their accumulation in wastewater may be associated with anthropogenic influences, such as agricultural and livestock practices. Prolonged exposure to antibiotics among inpatients may also have contributed to the observed high resistance rates.

In our study, the resistance rate of cephalosporins was found to be approximately 30%. Our country is included in The Central Asian and European Surveillance of Antimicrobial Resistance network (CESAR) and provides regular data. Antimicrobial resistance surveillance in Europe 2023 according to 2021 data Third-generation cephalosporin (cefotaxime, ceftriaxone, ceftazidime) resistance rates about 50% (29). Another studied show that resistance was detected against the antibiotics cefixime (38.2%), ceftriaxone (34.2%), ceftazidime (32.3%), and cefepime (29.6%) (30).

The limitations of our study are as follows: 1. The study is retrospective in nature. 2. The study is single-centred. 3. The study does not include anaerobes in bacterial classes. 4. The study lack ssusceptibility results for fungal infections.

CONCLUSION

It is very important to reveal the change in antibiotic resistance over time, especially when starting empirical treatment. We believe that these results will shed light on empirical treatments.

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