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The Isolates of Bacteriuria and Fungiuria: Single Center Laboratory-Based 14-Year Analysis

Bakteriüri ve Fungiüri İzolatları: Tek Merkezli Laboratuvara Dayalı 14 Yıllık Analiz

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ABSTRACT

Introduction: *Developing and changing medical practices may cause a change in the frequency, variety and susceptibility of infection agents over years. Therefore, the analysis reports of the isolates in urinary tract infections (UTIs) will provide significant contributions to the correct management of these infections. We aimed to analyze the trends of frequency, distribution and antimicrobial susceptibility of agents isolated from urine cultures of both ambulatory patients and inpatients in this study.*

Materials and Methods: *We evaluated the results of urine cultures for a 14-year period, retrospectively.*

Results: *A total of 49.034 isolates from 46.626 culture positive nonrepetitive specimens were included. The most common isolate was E. coli (46.2%), followed by Enterococcus species (12.2%). Significant differences in species distribution were observed based on gender and the units where patients were treated, including ambulatory care, inpatient units, and intensive care units. The highest susceptibility rates for E. coli were observed with imipenem (≥99%) and amikacin (≥86%). The susceptibility of E. coli to cefazolin decreased over the years (from 70% to 32%). Enterococcus spp. were susceptible to vancomycin and linezolid with high rates (≥92% and ≥95%, respectively). A prominent decrease was observed in the susceptibility rate for Enterococcus spp. against ampicillin in years; from 94% to 68%. A continuous decreasing trend was detected in the susceptibility of Klebsiella spp.*

Conclusion: *E. coli continues to be the most common urinary isolate. The distribution and frequency of isolates may show difference among centers and units. Continuous monitoring of antimicrobial susceptibility is important for accurate management of UTIs.*

Key Words: *Bacteriuria; Urine culture; Antimicrobial susceptibility; Species distribution*

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ÖZ

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Giriş: *Gelişen ve değişen tıbbi uygulamalar, yıllar içinde infeksiyon etkenlerinin sıklık, çeşitlilik ve duyarlılıklarının değişmesine neden olabilmektedir. Bu nedenle idrar yolu infeksiyonlarında (İYE) izolatların analiz raporları bu infeksiyonların doğru yönetimine önemli katkılar sağlayacaktır. Bu çalışmada, hem ayaktan hem de yatan hastaların idrar kültürlerinden izole edilen etkenlerin sıklık, dağılım ve antimikrobiyal duyarlılık eğilimlerini analiz etmeyi amaçladık.*

Materyal ve Metod: *On dört yıllık idrar kültürü sonuçlarını geriye dönük olarak değerlendirdik.*

Bulgular: *Çalışmaya, 46.626 kültür pozitif tekrarsız örnekten izole edilen toplam 49.034 izolat dahil edildi. En yaygın izolat Escherichia coli (%46.2) iken, bunu Enterococcus türleri (%12.2) izledi. Tür dağılımında, ayaktan hasta, yatan hasta ve yoğun bakım hastaları arasında ve cinsiyete göre önemli farklılıklar tespit ettik. E. coli için en yüksek duyarlılık oranları imipenem (≥%99) ve amikasine (≥%86) karşıydı. E. coli'nin sefazolin'e duyarlılığı yıllar içinde azaldı (%70'ten %32'ye). Enterococcus türleri vankomisin ve linezolide karşı yüksek oranlarda duyarlıydı (sırasıyla ≥%92 ve ≥%95). Enterococcus türlerinin ampisiline duyarlılığında yıllar içinde belirgin bir azalma gözlendi; %94'ten %68'e. Klebsiella spp. duyarlılığında sürekli bir azalma eğilimi saptandı.*

Sonuç: *E. coli en sık görülen üriner izolat olarak devam etmektedir. İzolatların dağılımı ve sıklığı merkezler ve birimler arasında farklılık gösterebilir. Antimikrobiyal duyarlılığın sürekli izlenmesi, İYE'lerin doğru yönetimi için önemlidir.*

Anahtar Kelimeler: *Bakteriüri; İdrar kültürü; Antimikrobiyal duyarlılık; Tür dağılımı*

INTRODUCTION

Bacteriuria or funguria are the presence of uropathogenic bacteria or fungi in the urine. Urinary tract infection (UTI) is a common worldwide infection caused by one or more of these organisms in any part of the urinary tract, including the urethra, bladder, ureters, or kidneys[1,2]. The most reliable method for detection is the isolation of these organisms through routine urine culture. Urinary tract infections are a significant cause of morbidity in both men and women of all ages. However, it is more prevalent among women, with nearly half of them experiencing a UTI at some point in their lives[1]. Serious sequelae include frequent recurrences, pyelonephritis, renal damage in children, pre-term birth and complications caused by frequent antimicrobial use, such as antimicrobial resistance and pseudomembranous colitis[3]. Furthermore, the urinary tract is a common source of Gram-negative bacteremia in hospitalized patients, which increases with age and gender[1,4]. It has been reported that the societal costs of these infections are approximately US $3.5 billion per year in the United States[3].

In general, the agents causing UTIs predominantly consist of the patient's own intestinal microbiota. These microorganisms account for the majority of isolates obtained from both hospitalized patients and ambulatory patients[5]. The microbial etiology of urinary tract infections, with *Escherichia coli* being the most commonly isolated agent, has been well-established for many years[6]. As a result, studies focusing solely on the frequency or distribution of uropathogens may have limited relevance. However, several factors such as changes in medical practices, increased intensive care unit (ICU) admissions and prolonged stays, aggressive antibiotherapy in ICUs, improved chemotherapy leading to longer life spans in cancer patients, rising rates of organ transplantations, and the global increase in the elderly population can contribute to changes in the frequency, diversity, and susceptibility of uropathogens over time. Moreover, the widespread use of broad-spectrum antibiotics and the ongoing challenge of antimicrobial resistance remain significant concerns on a global scale. Indeed, numerous reports have demonstrated increasing rates of resistance among various infectious agents[7-9]. Therefore, local or general analysis reports containing changes in species distribution and susceptibility characteristics of the isolates in urinary infections will provide significant contributions to the correct management of these common infections. In this study, our aim was to analyze the trends in the frequency, distribution, and antimicrobial susceptibility of agents isolated from urine cultures obtained from both ambulatory patients and inpatients over a span of 14 years.

MATERIALS and METHODS

We conducted a retrospective evaluation of all isolates obtained from urine cultures collected from both inpatients and outpatients across all departments of our hospital. The evaluation spanned a period of 14 years, from January 2006 to January 2020. This study was approved by the local ethics committee (13.07.2021/23). It was conducted in the microbiology laboratory of a 1000-bed tertiary university hospital. Annually, approximately 15.000-20.000 urine specimens are processed for culture examination in this laboratory. The processing and evaluation of routine urine cultures are performed according to Clinical Microbiology Procedures Handbook[5].

Procedures;

- All urine specimens were inoculated onto blood agar (BAP) and eosin methylene blue (EMB) agar.
- For specimens obtained from indwelling catheters, voided midstream urine, and pediatric urine collection bags, an inoculum of 0.001 mL (1 µL) was applied to each medium using sterile plastic loops. The inoculated plates were then incubated at 35°C for 24-48 hours.
- For other urine specimens obtained invasively or surgically, an inoculum of 0.01 mL (10 µL) was applied to each medium using sterile plastic loops. The inoculated plates were then incubated at 35°C for 48-72 hours.
- When one uropathogen grew at amount ≥10.000 CFU/mL or two uropathogens grew at amount ≥100.000 CFU/mL for each in the specimens of indwelling catheter and voided midstream urine, definitive identification and antimicrobial susceptibility testing (AST) were performed.
- Definitive identification and AST are conducted when one or two uropathogens are isolated at a concentration equal to or greater than 1000 CFU/mL, or when any pure culture of a lower count of uropathogen is found in other urine specimens obtained invasively or surgically.
- Vitek 2 (bioMerieux, Marcy l'Etoile, France) or BD Phoenix (BD Diagnostics, Sparks, MD) automated systems were used for identification and antimicrobial susceptibility testing.
- Antimicrobial susceptibility testing results were evaluated according to the Clinical and Laboratory Standards Institute (CLSI) until August 2015 and then European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines[10,11].

In cases where the same microbial agent was isolated in consecutive urine samples from the same patient within a one-month period, repetitive samples were excluded from the analysis, and only the first isolate was included. However, if the same microbial agent was isolated over a period of more than one month, it was considered as a different episode. For the purpose of this study, patients under the age of 18 years were included in the pediatric patients group.

SPSS Statistics software package was used for statistical analysis (IBM SPSS Statistics for Windows, Version 23.0 Armonk, NY). Chi-squared test was used to assess whether the prevalence of isolates differed among different groups. The level for statistical significance was determined as 0.05. Line graphics of antimicrobial susceptibilities were constituted to evaluate the changes in years by using Microsoft Excel program and the trends of changes were showed by trend lines.

RESULTS

Approximately 229.935 urine samples were processed for routine culture during the 14-year period, and out of these, 55.958 samples (24.3%) tested positive. A total of 46.626 culture positive nonrepetitive specimens were evaluated as significant and 49.034 isolates with identification and AST were included in this study. The most common isolate was *E. coli* with a rate of 46.2%, followed by *Enterococcus* species (12.2%) as the second most common agent (Table 1). The distribution of isolates did not exhibit any significant change in years.

Yeasts were the fourth most common isolates (9.8%) following the species of *E. coli*, *Enterococcus* and *Klebsiella* (Table 1). A total of 4680 (97.7%) *Candida* species and 108 (2.3%) non-*Candida* yeasts were isolated. Although the most frequent species was *C. albicans* (52.5%) in all *Candida* species, we observed that the rate of *C. albicans* was decreased in years (Figure 1).

When the distribution of isolates was evaluated according to gender, 32.250 (65.8%) were isolated from women, 16.784 (34.2%) were from men (Figure 2). Although the most common agent was *E. coli* for both genders, the distribution of isolates showed significant difference ($p< 0.005$). The second most common agents were *Enterococcus* spp. for men, and *Klebsiella* spp. for women. Most of the agents were isolated from adult patients (67.2%), 16.081 isolates (32.8%) were from pediatric patients. However, the distribution of isolates was almost similar among pediatric and adult patients, except for the isolates of yeasts, coagulase-negative staphylococcus (CoNS) and other enterobacteriaceae; yeasts were isolated more frequently from adult patients. *E. coli* was the most common uropathogen for both adult and pediatric patients, followed by yeast in adult patients and *Klebsiella* spp. in pediatric patients as the second most common agents (Figure 3).

Out of the total isolates, 19.660 (40.1%) were obtained from ambulatory patients, 23.156 (47.2%) from non-ICU hospitalized patients, and 6218 (12.7%) from ICU patients. We detected significant differences in the distribution of uropathogens among clinical units (the units of ambulatory patients, inpatients and ICU) of the center ($p< 0.005$). Although *E. coli* was also the most common agents in ambulatory patients (57.1%) and inpatients (43.4%), yeasts (29.8%), especially *Candida* spp. (n= 4683; 98% of yeasts), were the most common agents in ICU patients (Figure 4). Furthermore, the species of *Acinetobacter*, *Enterococcus*, and *Pseudomonas* were found to have significantly higher isolation rates in the ICU setting.

Polymicrobial growth was detected in 2403 (5.2%) of all urine specimens. The rates of polymicrobial growth among female and male patients were similar, 5.0% (n= 1541) and 5.4% (n= 862), respectively. The rates for adult and pediatric patients were also similar, 5.4% (n= 1665) and 4.8% (n= 738), respectively. However, polymicrobial growth rates in ICU patients and inpatients were higher than that of ambulatory patients; 6.8% (n= 396), 6.0% (n= 1380) and 3.2% (n= 627), respectively. The rate of polymicrobial growth in *Acinetobacter* spp. was the highest (18.7%) followed by *Klebsiella* spp., (16.7%) and *Pseudomonas* spp. (14.5%); the lowest rate was observed in *E. coli* (6.0%). Although the rate of polymicrobial growth in yeasts was 9%, concomitant growth rate of yeasts and *Enterococcus* spp. was 59% among polymicrobial growth including yeasts and bacteria. Furthermore, 72 polymicrobial growths contained two different yeast or two different *Candida* spp.

In vitro AST results are summarized in Figure 5. Although the highest susceptibility rates for *E. coli* were observed against imipenem (≥99%) and amikacin (≥86%), the lowest susceptibility rate was against ampicillin (<40%) (Figure 5A). The susceptibility of *E. coli* against cefazolin decreased over the years (from 70% to 32%). Vancomycin and linezolid were the drugs which *Enterococcus* spp. were most susceptible (≥92% and ≥95%, respectively) and the lowest susceptibility rate was detected with ciprofloxacin (≤52%) in vitro. A prominent decrease was observed in the susceptibility of *Enterococcus* spp. to ampicillin in years; from 94% to 68% (Figure 5B). Although the susceptibility of *Klebsiella* spp. to imipenem and amikacin were quite high, a trend of continuous decrease in the susceptibility of all drugs tested (imipenem, amikacin, ciprofloxacin, trimethoprim-sulfamethoxazole) was observed over the years (Figure 5C).

Table 1. Distribution of isolates over the years

Species	The rate of isolates over the years (n)														
	2006	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**Total**
E. coli	47.2 (1339)	49.4 (1305)	52.4 (1183)	46.2 (1287)	43.4 (1538)	43.0 (1593)	42.0 (1695)	45.5 (1438)	43.5 (1497)	46 (1556)	50.6 (1582)	50.4 (1844)	47.9 (2140)	44.7 (2676)	46.2 (22.673)
Enterococcus spp.	13.3 (377)	12.2 (323)	10.7 (242)	11.6 (323)	12.6 (447)	13.1 (485)	13.8 (558)	14.8 (466)	14.0 (482)	11.7 (397)	10.0 (314)	10.5 (386)	10.6 (473)	12.2 (729)	12.2 (6002)
Klebsiella spp.	9.2 (262)	10.3 (273)	10.2 (231)	14.7 (409)	12.3 (437)	11.9 (443)	11.0 (443)	10.4 (328)	10.5 (362)	10.5 (357)	11.7 (367)	13.4 (491)	13.7 (613)	12.5 (746)	11.8 (5762)
Yeasts	9.9 (281)	7.8 (206)	9.2 (208)	8.3 (232)	7.9 (280)	9.5 (352)	9.8 (395)	9.9 (312)	11.8 (406)	10.5 (356)	9.0 (282)	8.4 (308)	9.1 (406)	12.8 (764)	9.8 (4788)
CoNS	6.3 (179)	6.8 (180)	4.3 (97)	4.1 (113)	6.0 (214)	5.0 (187)	5.5 (220)	4.3 (135)	4.1 (141)	5.8 (195)	4.2 (132)	2.9 (108)	2.3 (104)	2.5 (149)	4.4 (2154)
Pseudomonas spp.	3.9 (112)	3.2 (85)	2.8 (63)	3.0 (83)	4.2 (148)	4.9 (182)	4.1 (165)	4.2 (134)	5.1 (174)	4.0 (136)	4.0 (125)	4.6 (167)	4.2 (189)	3.6 (214)	4.0 (1977)
Enterobacter spp.	2.1 (59)	1.8 (48)	2.6 (59)	3.6 (101)	3.4 (122)	3.5 (128)	2.6 (103)	1.6 (49)	2.4 (81)	2.4 (81)	2.6 (82)	1.9 (71)	3.0 (132)	2.3 (136)	2.6 (1252)
Proteus spp.	2.2 (61)	2.0 (54)	2.5 (56)	2.3 (65)	3.0 (108)	2.6 (96)	2.9 (118)	2.6 (82)	2.2 (77)	2.1 (71)	1.1 (34)	1.6 (60)	2.7 (121)	2.4 (141)	2.3 (1144)
Other Enterobacteriacae	1.3 (37)	1.6 (42)	1.9 (42)	1.6 (45)	1.9 (67)	2.0 (76)	2.6 (106)	2.1 (65)	1.8 (62)	2.4 (80)	2.7 (84)	1.9 (70)	2.1 (94)	2.5 (148)	2.1 (1018)
Acinetobacter spp.	1.7 (49)	2.0 (54)	1.5 (33)	2.6 (73)	2.4 (85)	2.1 (78)	2.1 (85)	1.6 (52)	1.7 (58)	1.6 (53)	1.8 (57)	1.9 (68)	1.6 (73)	1.9 (114)	1.9 (932)
S. aureus	1.2 (34)	1.7 (44)	1.0 (23)	1.0 (27)	1.6 (56)	1.2 (44)	1.5 (60)	1.6 (61)	1.2 (41)	0.9 (31)	0.9 (29)	0.7 (24)	1.0 (44)	0.8 (45)	1.1 (553)
Streptococcus spp.	1.1 (30)	0.7 (19)	0.6 (13)	0.6 (17)	0.4 (14)	0.5 (17)	1.5 (62)	0.9 (30)	1.4 (49)	1.7 (56)	0.8 (25)	1.4 (50)	1.3 (58)	1.5 (91)	1.1 (531)
Other nonfermentative bacteria	0.6 (17)	0.4 (10)	0.3 (6)	0.3 (8)	0.8 (30)	0.7 (27)	0.6 (26)	0.5 (16)	0.4 (14)	0.4 (15)	0.4 (13)	0.4 (15)	0.5 (22)	0.5 (29)	0.5 (248)
Total	5.8 (2837)	5.4 (2643)	4.6 (2256)	5.7 (2783)	7.2 (3546)	7.6 (3708)	8.2 (4036)	6.4 (3158)	7.0 (3444)	6.9 (3384)	6.4 (3126)	7.5 (3662)	9.1 (4469)	12.2 (5982)	49.034

Yeasts: Species of Candida, Trichosporon, Geotrichum, Saprochaeta.
Other Enterobacteriacae: Serratia, Morganella, Citrobacter, Providencia, Hafnia, Kluyvera, Pantoea, etc.
Other nonfermentative bacteria: Stenotrophomonas, Achromobacter, Burkholderia, Aeromonas, Sphingomonas, Alcaligenes, etc.

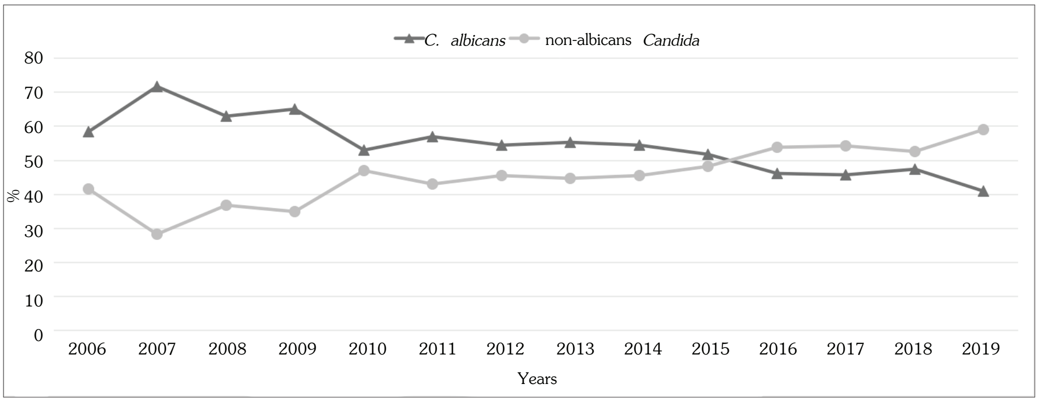


Figure 1. The frequency of *C. albicans* and non-*albicans Candida* isolates over the years.

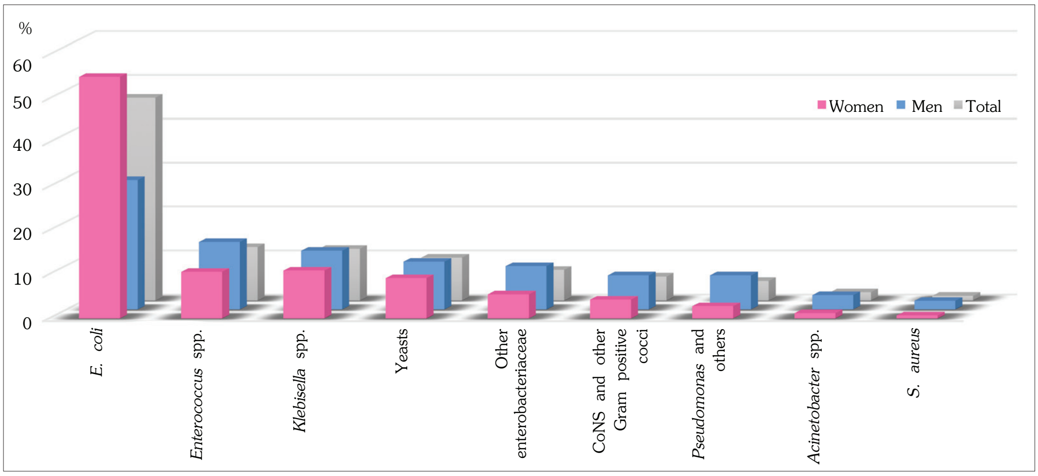


Figure 2. The distribution of isolates according to gender.

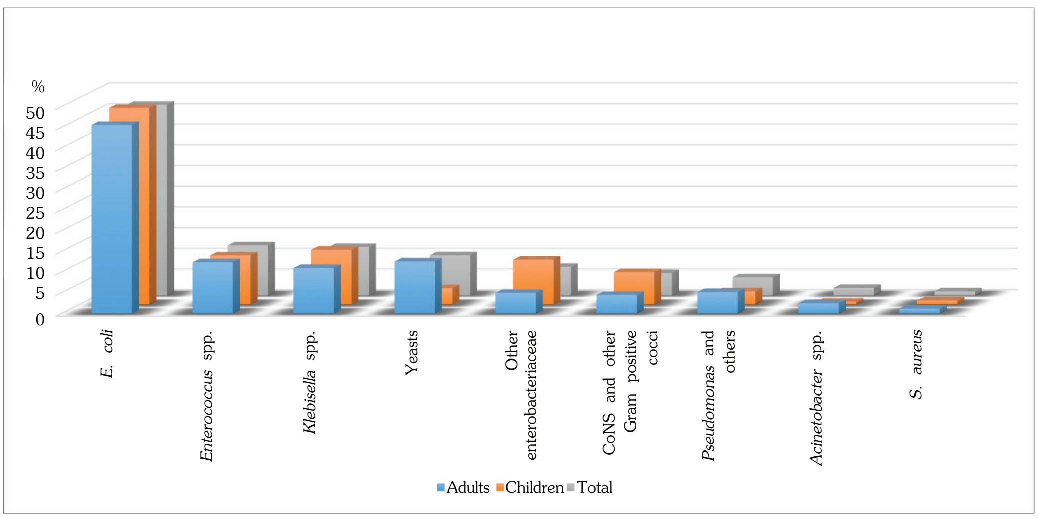


Figure 3. The distribution of isolates among pediatric and adult patients.

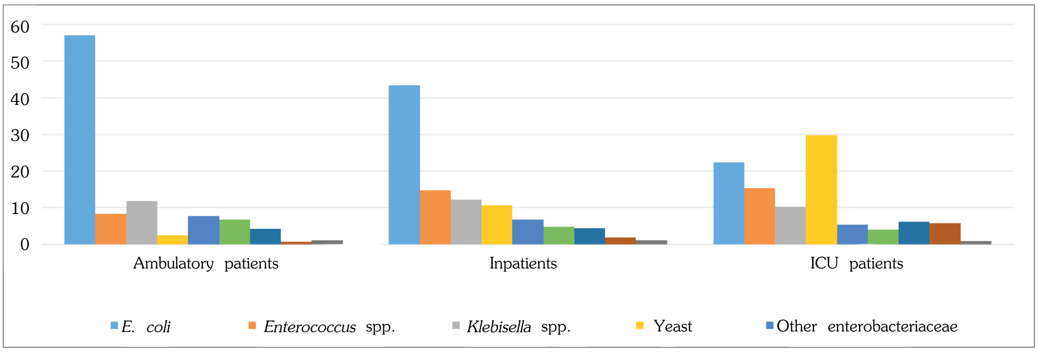


Figure 4. The distribution of uropathogens among clinical units.

The highest and an increasing susceptibility of CoNS was detected to trimethoprim-sulfamethoxazole (TMP-SMX; from 63% to 81%) (Figure 5D). We did not observe any apparent difference in the oxacillin susceptibility trend of CoNS in years; it ranged 21-40% (mean, 29%). The most prominent decrease in susceptibility of *Pseudomonas, Enterobacter, Proteus* and *Acinetobacter* was observed to piperacillin, cefepime, and imipenem, respectively (Figure 5E, F, G, H).

DISCUSSION

Urine is a normally sterile body fluid; however, it is easily contaminated with microbiota from perineum, prostate, distal urethra, or vagina. Therefore, microbial growth can be observed in routine urine culture without urinary tract infection. Because the laboratory rarely knows details about the patient except for age, and sex and type of specimen, the significance of bacteria in the urine is usually based only on the criterion of bacterial counts[5]. Therefore, urine specimens are routinely inoculated quantitatively, and the growth in culture is evaluated based on colony count in our laboratory.

The most commonly responsible species in UTI has been reported to be *E. coli* (≥70%) along with *Klebsiella* spp., *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp. and other enterobacteriales, accounting for most of the remaining isolates[12-14]. However, significant differences have also been reported in species distribution according to age, gender and location groups of patients[12,15]. The most common isolated species was *E. coli* from all patients in our laboratory with a less rate (46.2%) than previous reports[12,16-18]. Another apparent difference was the high rate of *Enterococcus* spp.; it was the second most common isolate in our center. *Enterococcus* spp. has been reported as the second most common causative agents for complicated UTIs, following uropathogenic *E. coli* as the most common[3]. In a multicenter retrospective study including pediatric patients, *Enterococcus* spp. were the second most common causative pathogens and male predominance, vesicoureteral reflux and recent antibiotic use were higher in patients with *Enterococcus* spp. than in those with *E. coli*[19]. We think that our high rate of *Enterococcus* spp. is due to the fact that our laboratory serves the patients in a tertiary care hospital. In addition, this analysis was conducted in a single center and species distribution may also exhibit differences among geographical regions. The isolation rate of *E. coli* was higher in women than men, and it was higher in ambulatory patients than inpatients and ICU patients. In women, the higher incidence of infection and the more frequent isolation of *E. coli* than men are explained by the anatomical structure and localization of the female urethra[15]. In a study including women with community-acquired urinary tract infection, isolation rate of *E. coli* was 53.5%[17]. In male patients, because of more frequent isolation rate of pathogens such as *Enterococcus, Acinetobacter, Pseudomonas, S. aureus*, the agents other than *E. coli* should also be considered in the management of UTIs. Agents isolated from children often consisted primarily of *E. coli*, along with *Klebsiella*, *Enterococcus*, and CoNS.

As expected, resistant nosocomial pathogens such as the species of *Enterococcus, Acinetobacter, Pseudomonas* and yeasts were more frequently isolated from hospitalized patients, es-

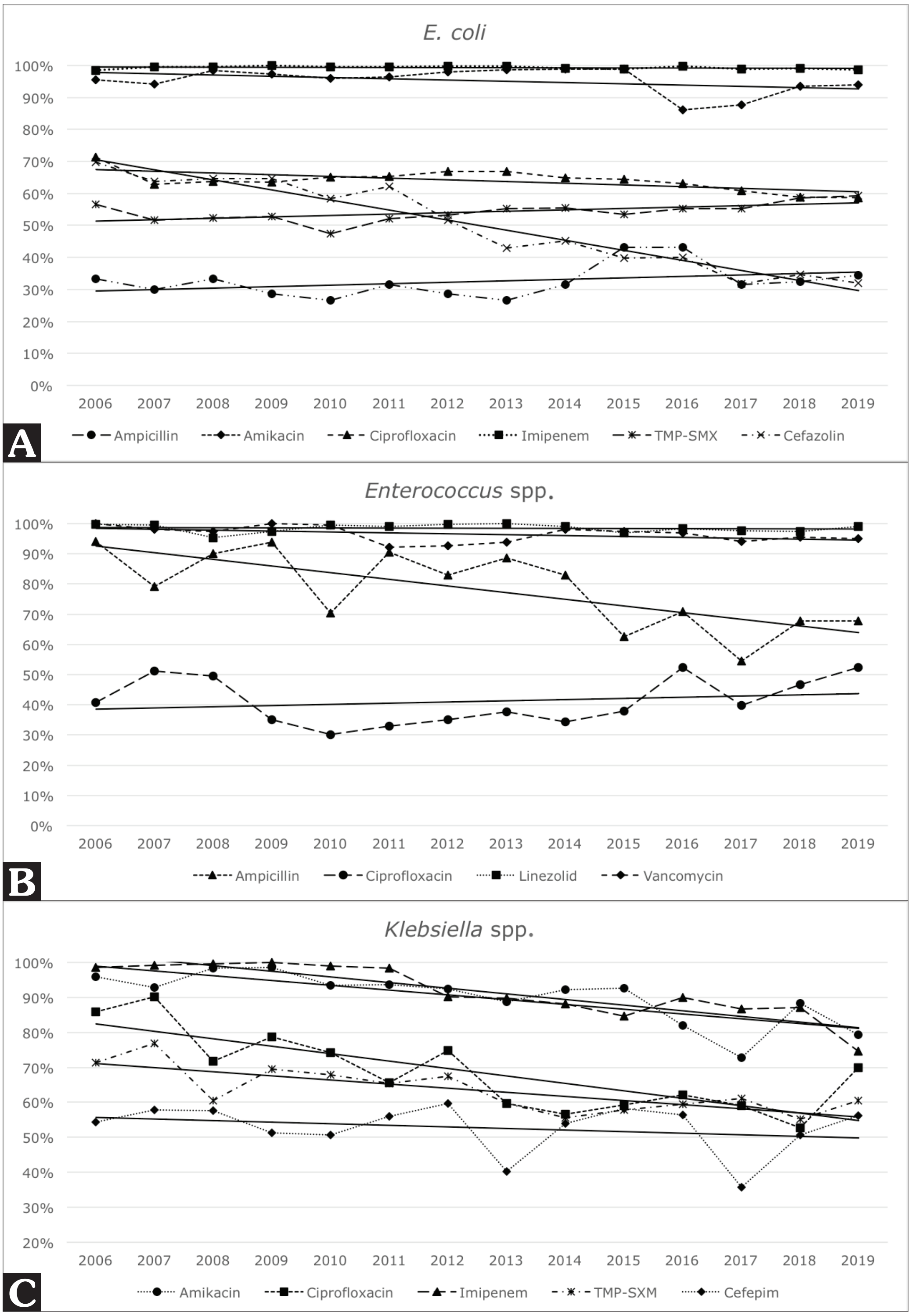
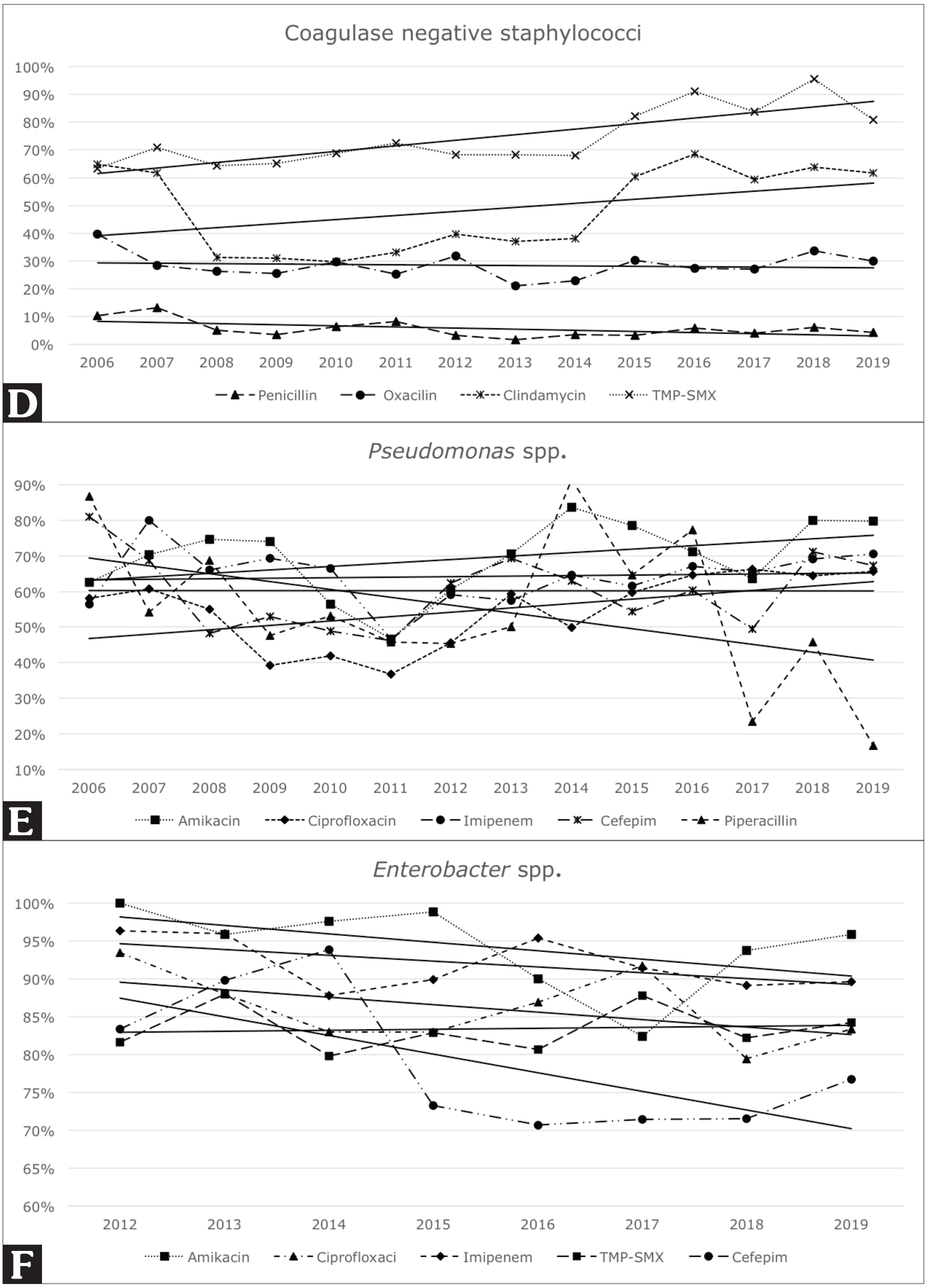


Figure 5. Antibacterial susceptibility testing results.
Line graphics of antimicrobial susceptibilities were constituted to evaluate the changes in years and the trends of changes were shown by trend lines.



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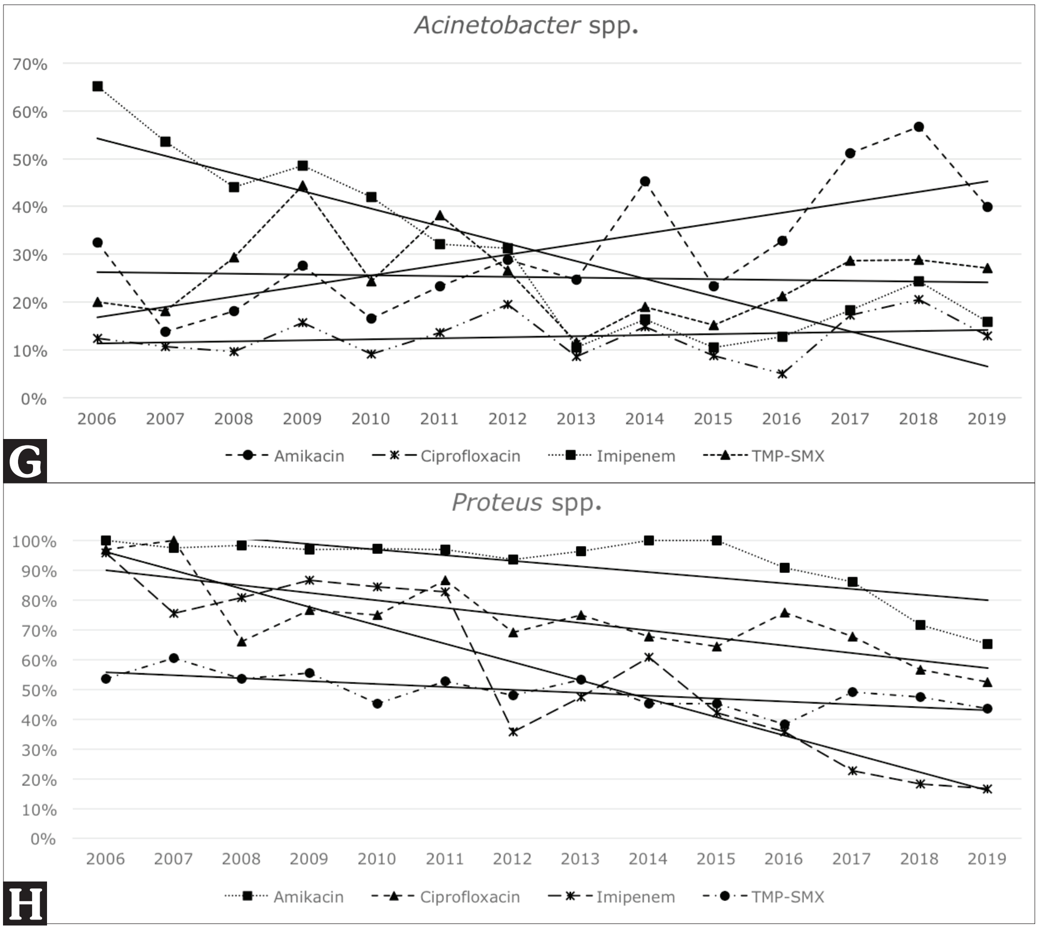

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pecially ICU patients. Furthermore, yeasts were the most common isolates that were isolated from urine cultures of ICU patients, followed by *E. coli* and *Enterococcus* species. This finding has been reported for catheter-associated UTIs previously[14,20]. When all of our intensive care unit patients are thought to have urinary catheters, our results support previous reports; *Candida* spp. are the most common etiological agents of UTIs in ICU patients and/or catheter-associated UTIs[14,20].

We detected polymicrobial growth in 5.2% of all urine specimen, similar to the results of Laupland et al.[12]. Polymicrobial growth was more frequent in hospitalized patients and in the presence of resistant organisms in culture. Even though urinary infections often have a monomicrobial etiology, urine cultures should be carefully evaluated in terms of polymicrobial infections. *Acinetobacter* spp. were the most inclined agents to polymicrobial growth. The most interesting finding in polymicrobial growth was the high frequency of association of *Enterococcus* spp. and yeasts. Therefore, when the presence of polymicrobial growth including yeast in any urine culture, the primary agent to be considered as the concomitant microorganism should be enterococci.

In this study, we also evaluated the susceptibility trends of bacterial isolates against antibacterial drugs. Almost all isolates of *E. coli* were susceptible to imipenem over the years. Similarly, the susceptibility rate to amikacin was high, but we detected a slight decrease in the susceptibility of amikacin and ciprofloxacin in years. We observed the lowest susceptibility rates against ampicillin and TMP-SMX in our analysis. Previously, high resistance rates were reported for community acquired uropathogenic *E. coli* against ampicillin and TMP-SMX throughout Europe and a clear increase in resistance to fluoroquinolones was recorded[17]. The retrospective analysis conducted by Sanchez et al.[18] demonstrated an increase in resistance to ciprofloxacin among *E. coli* isolates when comparing the years 2003 and 2012. The most apparent alteration was observed in the susceptibility rate of *E. coli* against cefazolin; decreased from 70% to 32% over the years. In a pediatric patient population, Wang et al.[21] reported the resistance rate for *E. coli* as 93.2% to ampicillin, 82.21% to cefazolin and 58.03% to TMP-SMX. In a retrospective analysis of 11.943 aerobic urine cultures for two different periods (2005-2006 vs 2010-2011) in a university hospital, the susceptibilities of cefazolin and ciprofloxacin decreased from 95.2% to 91.9% and from 92.9% to 84.9%, respectively[16]. Although it may appear that ampicillin, cefazolin, and TMP-SMX are not optimal choices for treating UTIs caused by *E. coli*, it is important to note that this conclusion might not be accurate. The susceptibility rates may vary depending on the source of infection, such as ambulatory patients versus inpatients, or complicated versus uncomplicated UTIs. Therefore, a separate evaluation of susceptibilities in these different patient groups is necessary to draw more accurate conclusions.

Enterococcus spp. were the second most common agents isolated from urine cultures in our laboratory. The susceptibilities to vancomycin and linezolid were extremely high for *Enterococcus* spp. and ampicillin susceptibility exhibited an apparent decrease. Wang et al.[21] showed that *Enterococcus* spp. were the most common bacteria leading to UTI in pediatric patients (n= 2316) in their center and resistance rates were 0.98% to vancomycin, 2.09% to linezolid, 49.02% to levofloxacin and 65.23% to ampicillin. Miranda et al.[16] reported decreased susceptibilities in two different periods (2005-2006 and 2010-2011); from 100% to 90.2% for ampicillin and from 98.6% to 97.3% for vancomycin. Our results support that the susceptibility of *Enterococcus* spp. to ampicillin has decreased over the years.

Previous reports demonstrated the trends of increasing resistance of *E. coli* and other uropathogenic bacteria to various classes of antimicrobial agents[18,22]. Continuous decreasing trends in the susceptibility of all drugs evaluated were observed over the years for the members of Enterobacteriaceae including the species of *Klebsiella*, *Enterobacter* and *Proteus* in this study. Furthermore, similar decreasing trends in the susceptibility of all urine isolates were observed against several antimicrobial drugs in the present analysis.

As this analysis is based on laboratory data only, it has several limitations. We did not have any clinical data such as sign and symptoms, antimicrobial therapy, underlying disorders, medical histories. Therefore, we could not make any classification about UTIs (complicated, uncomplicated, asymptomatic bacteriuria etc.). In addition, two different guides were used to evaluate AST, which may affect the susceptibility test results.

CONCLUSION

In conclusion, the most common agent isolated from urine specimens was *E. coli*, followed by *Enterococcus* spp. in our center. Almost two-thirds of the samples were from women. The distribution of isolates showed significant difference according to gender and clinical units of the center, yeasts were the most frequent agents in ICU. Although *E. coli* continues to be the most common urinary isolate, the distribution and frequency of isolates may show difference among centers and units. Even though the distribution of isolates did not differ over the years, decreases in susceptibility to some antimicrobial drugs were detected. As a result, when the previous reports of increases in resistance or decreases in susceptibility were also considered, continuous monitoring of antimicrobial susceptibility is important for proper therapeutic decision making and ultimately for the accurate management of UTIs. Furthermore, the wide range of microbial etiology and the lack of a single antimicrobial agent effective against all pathogens involved in UTIs highlight the importance of comprehensive testing, which includes isolation, identification, and antimicrobial susceptibility testing.

ETHICS COMMITTEE APPROVAL

This study was approved by Eskişehir Osmangazi University Non-Invasive Clinical Ethics Committee (Decision no: 23, Date: 13.07.2021).

CONFLICT of INTEREST

We declare that we have no financial, commercial, or other relationships that could potentially cause a conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: YÖ, GD

Analysis/Interpretation: All of authors

Data Collection or Processing: YÖ, NK, GS

Writing: YÖ, NK

Review and Correction: All of authors

Final Approval: All of authors

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