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RESEARCH ARTICLE/KLİNİK ÇALIŞMA

FLORA 2025;30(3):267-274 • doi: 10.5578/flora.2025031363

# Overlooked Urogenital Pathogens: Clinical Importance of *Mycoplasma hominis* and *Ureaplasma urealyticum* in Urine Samples

## Gözden Kaçabilen Ürogenital Patojenler: İdrar Örneklerinde *Mycoplasma hominis* ve *Ureaplasma urealyticum*'un Klinik Önemi

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***Cite this article as:*** *Gürler M, Kırca F, Çöplü N, Dinç B. Overlooked urogenital pathogens: Clinical importance of mycoplasma hominis and ureaplasma urealyticum in urine samples. FLORA 2025;30(3):267-274.*

### ABSTRACT

***Introduction:*** *Mycoplasma hominis and Ureaplasma urealyticum are uropathogens, especially in patients with genitourinary system disorders, but no urine culture growth. This study aimed to evaluate the presence of M. hominis and/or U. urealyticum in urine samples, antibiotic susceptibilities, and concurrent routine urine culture and urinalysis results.*

***Materials and Methods:*** *The results of 3042 patients were analyzed. Mycoplasma-IES (AutobioDiagnostics, China) kit was used to determine the culture and antibiotic-susceptibilities of M. hominis-U. urealyticum. Concomitant routine urine culture-urinalysis results were compared with M. hominis-U. urealyticum culture results.*

***Results:*** *The study evaluated 6084 results. M. hominis and/or U. urealyticum growth was detected in 17.1% of patients. The frequency of U. urealyticum was found to be higher. When antimicrobial resistance rates were analyzed, josamycin resistance was found to be significantly higher in individuals over 65 years of age with M. hominis and/or U. urealyticum positivity. Additionally, resistance to ciprofloxacin, levofloxacin, ofloxacin, clindamycin, and clarithromycin was significantly higher in females with U. urealyticum positivity. A significant difference was observed between M. hominis positivity and no growth in routine urine cultures compared to the presence of growth. A significant correlation was found between U. urealyticum positivity and the absence of growth in routine urine cultures, as well as negative findings on urinalysis.*

***Conclusion:*** *Although M. hominis and U. urealyticum are common commensal flora of the genitourinary system, it is clinically important to evaluate their presence on a case-by-case basis, considering their pathogenic potential.*

***Key Words:*** *Mycoplasma hominis; Ureaplasma urealyticum; Urine culture; Urinalysis*

Received/Geliş Tarihi: 20/03/2025 - Accepted/Kabul Ediliş Tarihi: 26/05/2025





Available Online Date: 25.09.2025

## ÖZ

### Gözden Kaçabilen Ürogenital Patojenler: İdrar Örneklerinde *Mycoplasma hominis* ve *Ureaplasma urealyticum*'un Klinik Önemi

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***Giriş:*** *Mycoplasma hominis ve Ureaplasma urealyticum, özellikle genitoüriner sistem (GÜS) şikayetleri olan ancak idrar kültüründe üreme saptanamayan hastalarda sık karşılaşılan üropatojenlerdendir. Bu çalışma, idrar örneklerinde M. hominis ve/veya U. urealyticum varlığını, antibiyotik duyarlılıklarını ve eş zamanlı gönderilen rutin idrar kültürü ve tam idrar tetkiki sonuçlarını değerlendirmeyi amaçlamaktadır.*

***Materyal ve Metod:*** *Çalışmaya 3042 hastanın sonuçları dahil edildi. M. hominis-U. urealyticum'un kültür ve antibiyotik duyarlılıklarını belirlemek için Mycoplasma-IES (AutobioDiagnostics, Çin) kiti kullanıldı. Eş zamanlı gönderilen rutin idrar kültürü ve tam idrar tetkiki sonuçları, M. hominis-U. urealyticum kültür sonuçları ile beraber değerlendirildi.*

***Bulgular:*** *Çalışmada toplam 6084 sonuç değerlendirildi. Hastaların %17.1'inde M. hominis ve/veya U. urealyticum üremesi tespit edildi. U. urealyticum sıklığının daha yüksek olduğu saptandı. Antimikrobiyal direnç oranları analiz edildiğinde; M. hominis ve/veya U. urealyticum pozitifliği olanlarda josamisin direncinin >65 yaş grubunda istatistiksel olarak anlamlı derecede daha yüksek olduğu tespit edildi; siprofloksasin, levofloksasin, ofloksasin, klindamisin ve klaritromisin direnci U. urealyticum pozitifliği olan kadınlarda istatistiksel olarak anlamlı derecede daha yüksek bulundu. M. hominis pozitifliği ile rutin idrar kültürlerinde üreme olmaması arasında, üreme varlığına kıyasla anlamlı bir fark bulundu. U. urealyticum pozitifliği ile rutin idrar kültürlerinde üreme olmaması ve tam idrar tetkikinde lökosit-lökosit esteraz yüksekliğinin olmaması arasında anlamlı bir ilişki bulundu.*

***Sonuç:*** *M. hominis ve U. urealyticum, GÜS'ün yaygın komensal flora üyeleri olmalarına rağmen patojenik potansiyelleri göz önünde bulundurularak hasta özelinde değerlendirilmeleri klinik açıdan önemlidir.*


***Anahtar Kelimeler:*** *Mycoplasma hominis; Ureaplasma urealyticum; İdrar kültürü; Tam idrar tetkiki*

## INTRODUCTION

*Mycoplasma hominis* and *Ureaplasma urealyticum* are the smallest known microorganisms that lack a cell wall. Although they are common commensals of the human genitourinary system (GUS), *M. hominis* and *U. urealyticum* have also been implicated in clinical disorders such as orchitis, prostatitis, and non-gonococcal urethritis.[1]. As causative agents of urethritis, they are uropathogens that should be considered, especially in patients with GUS disorders, but no growth in urine cultures. The prevalence of *M. hominis* and *U. urealyticum* may vary depending on age, gender, and various sociodemographic characteristics. While the prevalence of *M. hominis* in the GUS is 20-30%, the rate for *Ureaplasma* spp. has been reported to be around 80%[2]. Culture is the gold standard for diagnosis, and special media are required for their growth. Commercial kits for routine diagnosis, identification, and antibiotic susceptibility can provide results within 24 hours. There may be regional differences in the antibiotic resistance profiles of these microorganisms depending on the antibiotic use strategies of individuals and countries. In our country, data on the frequency of *M. hominis* and *U. urealyticum*, their antibiotic resistance rates, and their evaluation with concurrent urine culture/urinalysis are minimal.

This study aimed to retrospectively evaluate the frequency of *M. hominis* and/or *U. urealyticum* growth, antibiotic susceptibility rates, and their correlation with concurrent urine culture/urinalysis samples sent to Ankara Bilkent City Hospital, Microbiology Laboratory.

## MATERIALS and METHODS

### Study Design and Setting

This retrospective study was conducted at Ankara Bilkent City Hospital, a tertiary care center located in Ankara, the capital city of Türkiye. The hospital, with a bed capacity of 4050, serves as a major referral center for the region. Urine samples from patients with

suspected GUS infections were submitted to the microbiology laboratory between January 2020 and July 2024 for the detection of *M. hominis* and *U. urealyticum*.

**Patient Selection**

Patients of all ages and genders presenting with urinary system complaints were included in the study. In cases where multiple samples were received from the same patient, only the first sample demonstrating growth was considered for analysis to avoid duplication bias.

**Laboratory Procedures**

Detection of *M. hominis* and *U. urealyticum*, along with antibiotic susceptibility testing, was performed using the Mycoplasma-IES kit (Autobio Diagnostics, China). The samples were inoculated, incubated, and evaluated according to the manufacturer's instructions. The kit provided antibiotic susceptibility results for tetracycline and levofloxacin separately for both *M. hominis* and *U. urealyticum*, while additional antibiotics tested included pristinamycin, minocycline, josamycin, erythromycin, roxithromycin, clindamycin, ofloxacin, ciprofloxacin, and clarithromycin.

Antimicrobial susceptibility interpretations were made according to the Clinical and Laboratory Standards Institute criteria and the manufacturer's recommendations[3]. Given that *M. hominis* is intrinsically resistant to 14- and 15-membered macrolides (such as erythromycin, clarithromycin, and roxithromycin), susceptibility testing for these antibiotics was not performed on *M. hominis* isolates.

**Additional Laboratory Data**

Routine urine culture and urinalysis results were evaluated alongside the *M. hominis* and/or *U. urealyticum* culture findings. Routine urine cultures were assessed following the guidelines of the Turkish Specialty Society of Clinical Microbiology for the laboratory diagnosis of urinary specimens[4]. Urinalysis was conducted using the Atellica 1500 Automated Urine Analysis System (Siemens, Germany), with a positive result indicated by a leukocyte count above five and the presence of leukocyte esterase.

**Data Collection and Statistical Analysis**

Demographic variables (age, gender), clinic of origin, and seasonal distribution of positive samples were recorded. Statistical analysis was conducted using SPSS version 22.0 (SPSS, United States of America). Descriptive statistics were used to show variable distribution and homogeneity. Continuous variables were presented as median (min-max), and categorical variables were analyzed using Chi-square or Fisher's exact tests for group comparisons. A value of $p< 0.05$ was considered statistically significant.

**Ethical Approval**

The ethical approval was obtained from the Ankara Bilkent City Hospital Medical Research Scientific and Ethical Review Board No.1 (October 23, 2024, no: TABED 1/672/2024).

**RESULTS**

In the study, a total of 6084 results were evaluated for the identification of *M. hominis* and *U. urealyticum* in urine samples, with 21% (643) from female patients and 79% (2399) from male patients. Of the samples, 83% (2521) showed no growth, while 16.1% (490) tested positive for *U. urealyticum*, 0.2% (9) for *M. hominis*, and 1% (22) for *M. hominis* + *U. urealyticum* co-infection. The frequency of *U. urealyticum* was found to be statistically significantly higher ($p< 0.001$). Patients with *M. hominis* and/or *U. urealyticum* positivity were referred from urology, infectious diseases, and internal medicine outpatient clinics, respectively. The demographic characteristics of the patients are provided in Table 1. *M. hominis* and/or *U. urealyticum* (521/3042) were detected in 25.7% of females (165/643) and 14.9% of males (356/2399).

While there was no significant difference in terms of gender in patients with *M. hominis* positivity ($p= 0.36$), *M. hominis* positivity was found to be statistically significantly higher in the 16-40 age group ($p< 0.001$). *U. urealyticum* positivity was significantly higher in the 16-40 age group and males ($p< 0.01$). When the distribution of the causative agents according to the seasons was examined, it was observed that

**Table 1. Demographic data of patients with *M. hominis* and/or *U. urealyticum* positivity**

| | *M. hominis* (n= 9) | | *U. urealyticum* (n= 490) | | Co-infection (*M. hominis* + *U. urealyticum*) (n= 22) | |
|---|---|---|---|---|---|---|
| Age groups | Female (n= 3) | Male (n= 6) | Female (n= 152) | Male (n= 338) | Female (n= 10) | Male (n= 12) |
| 0-15 years, n (%) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| 16-40 years, n (%) | 2 (67) | 6 (100) | 92 (60) | 276 (82) | 5 (50) | 10 (83) |
| 41-65 years, n (%) | 1 (33) | 0 (0) | 53 (35) | 60 (18) | 3 (30) | 2 (17) |
| >65 years, n (%) | 0 (0) | 0 (0) | 7 (5) | 2 (1) | 2 (20) | 0 (0) |

*M. hominis* was frequently detected in the fall (38.7%) and *U. urealyticum* was detected in the spring-summer months (58.8%).

The resistance rates for ciprofloxacin, clindamycin, josamycin, ofloxacin, levofloxacin, and tetracycline were 61.3%, 58.1%, 9.7%, 22.6%, 35.5% and 9.7% for *M. hominis* and 78.3%, 69.9%, 2.3%, 55.1%, 35.1%, 35.5% and 15.8% for *U. urealyticum*, respectively. Additionally, resistance rates for erythromycin, clarithromycin, and roxithromycin evaluated only in *U. urealyticum* isolates were 14.8%, 13.7%, and 12.5%, respectively (Table 2). When antimicrobial resistance rates according to age and gender were analyzed, *M. hominis* and/or *U. urealyticum* growth were most frequently detected in males between the ages of 16-40. However, among those with *M. hominis* and/or *U. urealyticum* positivity, josamycin resistance was found to be statistically significantly higher in the >65 age group ($p< 0.001$; $p= 0.002$, respectively), while *U. urealyticum* positivity, ciprofloxacin, levofloxacin, ofloxacin, clindamycin,

**Table 2. Antimicrobial resistance rates by age and gender**

| | | *M. hominis* (n= 31) | | | *U. urealyticum* (n= 512) | | |
|---|---|---|---|---|---|---|---|
| Antibiotic | Gender | 16-40 age | 41-65 age | >65 age | 16-40 age | 41-65 age | >65 age |
| Ciprofloxacin n, (%) | F | 3 (43) | 4 (100) | 2 (100) | 83 (86) | 49 (87) | 8 (89) |
| | M | 9 (56) | 1 (50) | 0 (0) | 220 (77) | 39 (63) | 2 (100) |
| Levofloxacin n, (%) | F | 1 (14) | 1 (25) | 2 (100) | 37 (38) | 32 (57.1) | 4 (44) |
| | M | 7 (44) | 0 (0) | 0 (0) | 87 (30) | 20 (32.2) | 2 (100) |
| Ofloxacin n, (%) | F | 0 (0) | 2 (50) | 2 (100) | 63 (65) | 45 (80) | 5 (55) |
| | M | 3 (19) | 0 (0) | 0 (0) | 142 (50) | 26 (42) | 2 (100) |
| Josamisin n, (%) | F | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 2 (22) |
| | M | 1 (6) | 0 (0) | 0 (0) | 8 (3) | 2 (3) | 0 (0) |
| Clindamycin n, (%) | F | 3 (43) | 4 (100) | 2 (100) | 73 (75) | 46 (82) | 9 (100) |
| | M | 8 (50) | 1 (50) | 0 (0) | 190 (66) | 40 (64) | 1 (50) |
| Tetracycline n, (%) | F | 0 (0) | 1 (25) | 1 (50) | 12 (12) | 6 (11) | 3 (33) |
| | M | 1 (6) | 0 (0) | 0 (0) | 49 (17) | 11 (18) | 0 (0) |
| Erythromycin n, (%) | F | * | * | * | 18 (18) | 10 (18) | 2 (22) |
| | M | * | * | * | 37 (13) | 9 (14) | 0 (0) |
| Clarithromycin n, (%) | F | * | * | * | 22 (23) | 9 (16) | 2 (22) |
| | M | * | * | * | 32 (11) | 5 (8) | 0 (0) |
| Roxithromycin n, (%) | F | * | * | * | 15 (15) | 6 (11) | 2 (22) |
| | M | * | * | * | 33 (11) | 8 (13) | 0 (0) |

and clarithromycin resistance were statistically significantly higher in females (p= 0.002; p= 0.002; p< 0.001; p= 0.003; p= 0.003, respectively).

When evaluating the concomitant routine urine culture and urinalysis orders of patients with *M. hominis* and/or *U. urealyticum* positivity, it was discovered that the rate of growth in routine urine cultures was 7% in *M. hominis* and 10% in *U. urealyticum*, while the rate of positive urinalysis was 52% in *M. hominis and* 28% in *U. urealyticum* (Figure 1). A significant difference was observed between *M. hominis* positivity and the absence of growth in urine cultures compared to the presence of growth (p< 0.001). Additionally, a significant correlation was found between *U. urealyticum* positivity and no growth in routine urine cultures, as well as no positive urinalysis (p< 0.001, p< 0.001, respectively).

Due to the retrospective design of the study and limitations of the hospital information system, detailed clinical symptoms of the patients could not be systematically evaluated.

## DISCUSSION

In this retrospective study, we evaluated the prevalence of *M. hominis* and *U. urealyticum* and their antimicrobial resistance patterns in urine samples collected over a five-year period. *M. hominis* and/or *U. urealyticum* growth was detected in 17.1% of patients with suspected GUS infections. Previous studies reported positivity rates for these pathogens ranging between 30% and 69% across various sample types such as urine, vaginal swabs, and endocervical swabs[5,6]. The use of different clinical sample types in earlier studies may explain the higher detection rates compared to our findings.

Consistent with our results, Kechagia et al. also reported that *U. urealyticum* was predominant, being detected in 98.3% of positive urine samples either alone or as part of a co-infection with *M. hominis*[7].

Consistent with our research, previous studies have also reported a higher prevalence of *M. hominis* and *Ureaplasma* spp. in females[5,8]. When analyzing the gender distribution among patients with *M. hominis* and/or *U. urealyticum*

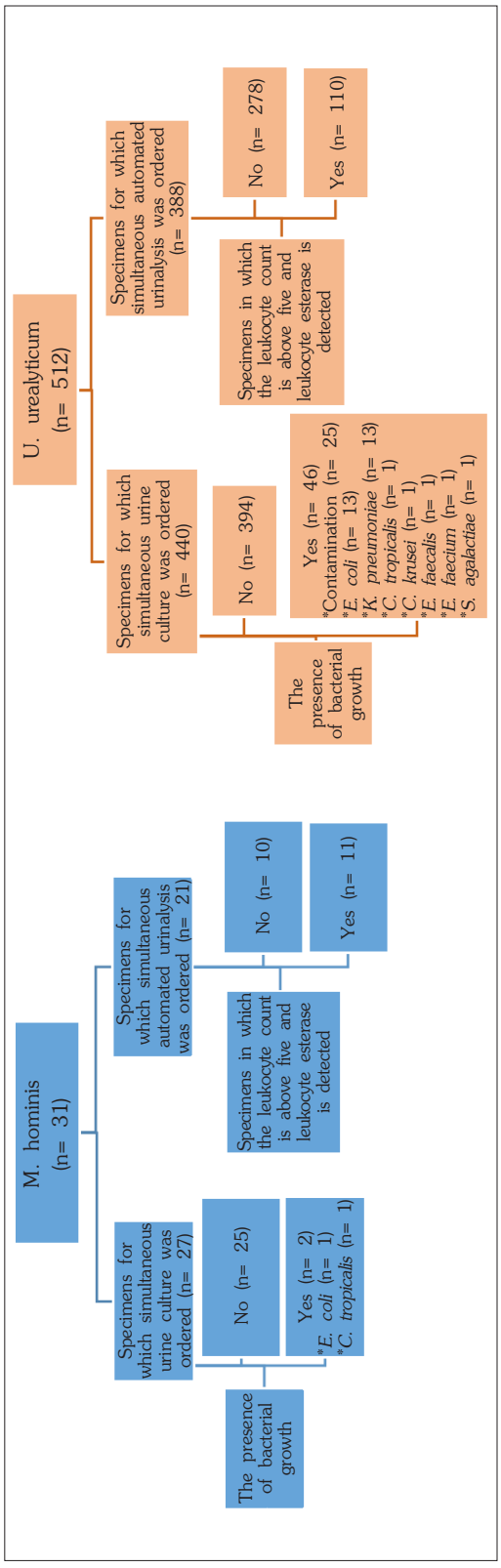


**Figure 1.** Evaluation of concurrent urine culture and urinalysis orders for patients with *M. hominis* and/or *U. urealyticum* positivity.
*E. coli: Escherichia coli, C. tropicalis: Candida tropicalis, K. pneumoniae: Klebsiella pneumoniae, C. krusei: Candida krusei, E. faecalis: Enterococcus faecalis, E. faecium: Enterococcus faecium, S. agalactiae: Streptococcus agalactiae.*

positivity, approximately 68% were female in the previous studies[5,8]. In the present study, 68% of the patients were male. This discrepancy may be due to differences in gender distributions within the populations studied.

Seasonal variations were also observed. Although earlier research indicated that detection rates were higher in winter months, we found that *M. hominis* was most frequently detected in the fall (38.7%), whereas *U. urealyticum* was more commonly identified during spring and summer (58.8%)[9]. Socioeconomic factors, regional cultural practices, hygiene behaviors, and sexual activity patterns are likely contributors to these seasonal variations. Moreover, curfews and other pandemic-related restrictions during the COVID-19 pandemic, which overlapped with nearly half of the study period, may have influenced the frequency and seasonal distribution of these infections[10].

Quinolones, tetracyclines, and macrolides are generally preferred for the treatment of mycoplasma infections. The resistance rate for ciprofloxacin, which has the highest resistance rate among quinolone group antibiotics, was 61.3% in *M. hominis* and 78.3% in *U. urealyticum*. In studies, the ciprofloxacin resistance rate for *M. hominis* strains was 23-96%[11,12], while the resistance rates for *U. urealyticum* varied between 51-93%[2,11]. In our study, the levofloxacin resistance rate was 35.5% for both microorganisms. A study conducted in our country reported a resistance rate of 26% for *M. hominis* and 15% for *U. urealyticum*[9]. In our research, the ofloxacin resistance rate was 22.6% in *M. hominis* and 55.1% in *U. urealyticum*, compared to rates ranging between 21-70% for *M. hominis* and 14-64% for *U. urealyticum* in other studies[12,13].

Among the tetracycline group antibiotics, the resistance rates for tetracycline were 9.7% for *M. hominis* and 15.8% for *U. urealyticum*. Previous studies have reported tetracycline resistance rates to vary between 17-58% for *M. hominis* and 6-50% for *U. urealyticum*[11,12,14].

As expected, *M. hominis* exhibited inherent resistance to 14- and 15-membered macrolides (erythromycin, clarithromycin, roxithromycin); therefore, susceptibility testing for these antibiotics was not conducted. In contrast, resistance to macrolides among *U. urealyticum* isolates was relatively low, with rates of 14.8% for erythromycin, 13.7% for clarithromycin, and 12.5% for roxithromycin. These findings align with previously reported rates of 2-46% across different regions[8,12,13]. A study conducted in Greece found no josamycin resistance in either *M. hominis* or *U. urealyticum*[7]. In our study, josamycin resistance was 9.7% in *M. hominis* and 2.3% in *U. urealyticum*, similar to other reports from Türkiye, despite the drug not being routinely available in our country[13,14].

Differences in resistance rates across studies may be explained by variations in regional antibiotic usage practices and local prescribing habits.

When antimicrobial resistance rates were analyzed by age and gender, it was discovered that josamycin resistance was significantly higher in the age group over 65 years for patients with *M. hominis* and/or *U. urealyticum* positivity ($p< 0.001$; $p= 0.002$, respectively).

In patients with *U. urealyticum* positivity, resistance to ciprofloxacin, levofloxacin, ofloxacin, clindamycin, and clarithromycin was found to be statistically significantly higher in females ($p= 0.002$; $p= 0.002$; $p< 0.001$; $p= 0.003$; $p= 0.003$, respectively).

When the routine urine culture and urinalysis of patients positive for *M. hominis* and/or *U. urealyticum* -submitted simultaneously- were evaluated, a significant difference was observed between *M. hominis* positivity and absence of growth in urine cultures compared to the presence of growth ($p< 0.001$). Additionally, microorganisms such as *E. coli*, *K. pneumoniae*, *Enterococcus* spp., and *Candida* spp. were also detected in a limited number of routine urine cultures. These findings were recorded descriptively and were not subjected to further statistical analysis, as the primary focus of the study was on *M. hominis* and *U. urealyticum*.

These findings suggest that urogenital *Mycoplasma* should be considered the causative agent in patients with positive urinalysis but no growth in routine urine culture.

However, there was a significant difference between *U. urealyticum* positivity and the absence of growth in urine cultures and the absence of positive urinalysis according to the presence of growth/positive urinalysis ($p< 0.001$, $p< 0.001$, respectively). These findings imply that *U. urealyticum* is frequently a colonizer rather than a true pathogen within the genitourinary system.

Consistent with our study, a systematic review including studies from Slovenia, Italy, India, and England found an association between *U. urealyticum* and genital disease in only one out of six studies[1]. Nevertheless, other studies have suggested that *U. urealyticum* may play a pathogenic role in conditions such as chronic prostatitis, urethritis, and infertility [15-17].

Thus, while *U. urealyticum* carriage is often asymptomatic, it may have clinical significance in selected patient groups, particularly in the absence of alternative etiologic agents. However, despite the detection of *M. hominis* and *U. urealyticum* in urine samples, the definitive causality in urinary tract infections cannot be established based solely on our findings due to the lack of comprehensive clinical and laboratory data.

In the study, we analyzed the growth of *M. hominis* and *U. urealyticum*, as well as antimicrobial resistance patterns in urine samples in Türkiye over a period of approximately five years. However, there are still some limitations to this study. First, since this is a retrospective study, the results mostly depend on the accuracy of the hospital data. Second, in our study, routine urine culture or urinalysis was not requested simultaneously with the urine samples sent for the investigation of the presence of *M. hominis* and *U. urealyticum* growth. Therefore, the relationship between *M. hominis* and *U. urealyticum* culture and routine urine culture and/or urinalysis could not be established for all samples. We believe that designing prospective studies in cooperation with relevant clinics will facilitate the clarification of this issue.

Additionally, detailed clinical symptom data were not available due to the retrospective nature of the study and the reliance on electronic medical records, which may not always accurately reflect the patients' presenting complaints.

Furthermore, since comprehensive clinical findings such as patient symptoms, physical examination results, or additional laboratory parameters could not be systematically reviewed, it is not possible to definitively conclude that *M. hominis* and *U. urealyticum* were the direct causative agents of urinary tract infections in the studied patients.

This study retrospectively analyzed the prevalence and antibiotic susceptibility profiles of *M. hominis* and *U. urealyticum* in urine samples collected between 2020 and 2024 in Ankara, Türkiye, alongside concurrent urine culture and urinalysis results. *U. urealyticum* was isolated more frequently than *M. hominis* and *M. hominis/U. urealyticum* co-infections. Additionally, both pathogens were more commonly detected in males aged 16 to 40 years.

Antimicrobial resistance rates for *M. hominis* and *U. urealyticum* varied across different antibiotic groups and showed regional differences compared to international data, highlighting the necessity for ongoing surveillance of resistance patterns in our country.

Although *M. hominis* and *U. urealyticum* are recognized members of the commensal flora of the genitourinary tract, their potential pathogenic roles should not be overlooked, especially in the appropriate clinical context. However, given the retrospective nature of the study and the absence of detailed clinical data, the association between these organisms and urinary tract infections must be interpreted with caution.

Further prospective studies combining microbiological findings with comprehensive clinical evaluations are essential to better elucidate the true pathogenic potential and clinical significance of these microorganisms.

## ETHICS COMMITTEE APPROVAL

The ethical approval was obtained from the Ankara Bilkent City Hospital Medical Research Scientific and Ethical Review Board No.1 (October 23, 2024, no: TABED 1/672/2024).

## CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

## AUTHORSHIP CONTRIBUTIONS

Concept and Design: MG, FK

Analysis/Interpretation: MG

Data Collection or Processing: MG

Writing: MG, FK

Review and Correction: All of authors

Final Approval: All of authors

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