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RESEARCH ARTICLE

Mycoplasma Hominis and *Ureaplasma Urealyticum* from the Perspective of the Microbiologist; Preferences, Prevalence and Antibiotic Susceptibility As a Test

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ABSTRACT

Objective: We aimed to investigate the incidence of *Mycoplasma hominis* and *Ureaplasma urealyticum* according to age and gender and the reasons why clinicians are asked to test them. We also defined their antimicrobial susceptibility.

Materials and Methods: The characteristics of 436 patients who were requested to have Mycoplasma and Ureaplasma tests between March 2021 and March 2022 were retrospectively analyzed. The complaints of each patient, the clinic to which they applied, and other simultaneously requested urine culture, vaginal culture, urine microscopy, and urine leukocyte strip test results were evaluated individually. Antimicrobial susceptibility was evaluated for the growing *U. urealyticum* and *M. hominis* tests.

Results: Testing was requested for a total of 436 patients with suspicion of *U. urealyticum* and *M. hominis* infection in a 1-year period. 94.9% of the patients, with a mean age of 38.2, had chronic urinary tract complaints. 71.1% were female, and 28.8% were male. Reproduction occurred in 30.2% of all patients. And 28.8% were *U. urealyticum* and 1.3% were *M. hominis*. Of all reproducing Ureaplasmas, 80.3% were female and 20 15.1% were male. Both urinary leukocyte microscopy and leukocyte strip testing were performed in only 204 of all patients. Mycoplasma and Ureaplasma test requests were investigated by the infectious diseases clinic in 86.6% of cases, mostly in patients with urinary complaints and urine material. *U. urealyticum* In the antimicrobial test, Pristinamycin and minocycline (98.4%), josamycin, roxithromycin, and erythromycin (100%), clarithromycin (96.7%), tetracycline (92%), levofloxacin (71.4%), ciprofloxacin (6.3%), clindaxacin (6%), 3 ofloxacin (15.8%) were found to be sensitive. A few (only six) Mycoplasma isolates were fully susceptible (100%) to tetracycline, minocycline, pristinamycin, and josamycin, while susceptibilities to other antimicrobial agents ranged mainly in the "moderate" or "resistant" range.

Conclusion: Test requests for Mycoplasma and Ureaplasma from patients are rare in our hospital, except for chronic urinary complaints. It is recommended to consider other diseases that may be caused for these microorganisms and to request laboratory tests from our laboratory for diagnosis and treatment. In addition, clinicians should request antimicrobial tests of these microorganisms, apply rational drug use, and avoid excessive antibiotic use.

Keywords: Antimicrobiyal susceptibility, *mycoplasma hominis*, *ureaplasma urealyticum*, uriner truct infections

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INTRODUCTION

Human-associated *Ureaplasma* and *Mycoplasma* are 0.2–0–3 µm in diameter, have coccoid forms, and are devoid of cell walls. Although they do not have a cell wall, they are pleomorphic, gram-negative, facultative anaerobes resistant to beta-lactam antimicrobials.[1–3] These bacteria need nucleic acid products and sterols for growth in a growth medium. In the growth medium, *Mycoplasma* make colonies with a diameter of 15–300 µm, which spread out toward the hollow edge, while *Ureaplasma* make colonies 15–60 µm in diameter that are noticeable under the microscope. Approximately 21–53% of asymptomatic sexually active women are colonized with *Mycoplasma* in the cervix or vagina, although the incidence is slightly lower

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in the male urethra.[4] *Mycoplasma hominis* is often associated with *Ureaplasma* species and can be transmitted sexually and vertically. Systemic infections are sometimes seen in newborns, older children, and adults. Such extragenital infections outside the neonatal period are usually, but not always, associated with an immunocompromised host state. Infections can sometimes cause adverse effects. Damage to the uterus, ovaries, and fallopian tubes is called pelvic inflammatory disease (PID). *Mycoplasma* and infections also cause infertility problems in women by causing permanent damage to the fallopian tubes and uterus. *Mycoplasma* and *Ureaplasma* cause urinary tract inflammation (urethritis) in men. These bacteria can cause discharge and burning with urination, as well as prostate infections. They can also make it difficult to have children by impairing sperm count and movement. *Mycoplasma* and *Ureaplasma* can also cause sexually transmitted diseases. They can be transmitted from the genital area to the genital area of the partner or from the genital area to the mouth by oral sex. The effects of diseases that occur, especially in women and men with weak immune systems and in newborns, are quite great. Timely diagnosis and treatment are important. Clinicians should not consider these microorganisms as a last resort when diagnosing their patients.[1,4] Detection of *Ureaplasma urealyticum* and *M. hominis* by culture methods is still the gold standard in microbiology laboratories.[1] However, commercial kits that allow *Ureaplasma* to be visually identified by color changes in the wells and that detect antimicrobial susceptibility by affecting pH by producing urease and anhydrous ammonia (NH3) have been developed and are used in many laboratories.

In our study, all patients for whom *M. hominis* and *U. urealyticum* tests were requested between March 2021 and March 2022 were included. Patients' complaints were evaluated with the clinics that requested the tests. Simultaneously, urine culture, vaginal culture, urethral culture, urine microscopy, and urine leukocyte strip tests were investigated, and patients were classified according to the reasons for demand, clinical factors, age, and sex. Antimicrobial tests were performed for those with *Mycoplasma* and *Ureaplasma*, and the results were evaluated. All information was obtained retrospectively from the automated hospital system.

MATERIALS and METHODS

In our study, 436 patients who had tests requested for *M. hominis* and *U. urealyticum* between March 2021 and March 2022 were retrospectively examined, with the approval of the Ethics Committee of Başakşehir Çam and Sakura City Hospital (November 17, 2021, no. KAEK/2021.11.246). Age groups were classified as 18–40 years (young adults), 41–65 years (adults), and over 65 years.

The *Mycoplasma* IES kit (Autobio Diagnostics, Brussels, Belgium) was used for testing. The process was as follows: the kits had 30 wells each. Twenty-five wells were prepared as strips of different concentrations of 11 different antimicrobials. There were positive control wells for *U. urealyticum* and *M. hominis* that contained arginine and urea, which are growth factors. Lincomycin was contained in *U. urealyticum* and erythromycin in *M. hominis* wells. There was only one well for pristinamycin. NH3 is released due to arginase in *M. hominis* and urease in U.urealyticum. NH3 changes the yellow color to pink-red by increasing the pH value in the well. This color change indicates reproduction. Pink-red coloration of *U. urealyticum* occurred in 104 wells; pink-red coloration of *M. hominis* occurred in 104 wells; and pink-red coloration of wells of *Mycoplasma* indicated growth of both microorganisms. A pristinamycin well with a single concentration was reported as susceptible if it was yellow and resistant if it was red. For antimicrobials with two concentrations, both wells were reported as susceptible (S) if they were colored yellow, moderately susceptible (I) if one well was yellow, and resistant (R) if both wells were red. The wells had separate antibiotic concentrations of tetracycline and levofloxacin for *M. hominis* and *U. urealyticum*. Other antibiotics were pristinamycin, minocycline, josamycin, erythromycin, roxithromycin, clindamycin, ofloxacin, ciprofloxacin, and clarithromycin.

Urine, vaginal, and urethral cultures were evaluated according to the laboratory diagnostic guidelines for urinary system samples recommended by clinical microbiology specialists.

The presence of five or more leukocytes in each area in the urine microscopy was considered positive. Urine microscopy and urine strip tests were performed completely automatically on the Cobas 6500 (Roche Diagnostics, San Francisco, USA) device.

Statistical Analysis

All analyses were performed using SPSS v25 (SPSS Inc., Chicago, IL, USA). Data were given as medians (min–max) for continuous variables and as frequencies (percentages) for categorical variables.

RESULTS

Of 436 patients with a mean age of 38.2 years (min 19–max 89), 71.1% (310/436) were female and 28.8% (126/436) were male (Table 1).

Table 1. Characteristics of the patients included in the study

	Average			Median			Min-max					
Age	38.2			44.5			19-89					
	Female			Male			Total					
	n		%	n		%						
Number of patients	310		71.1	126		28.8	n=436					
	18–40 years			41–65 years			>65					
	n		%	n		%	n		%			
	260[a]		59.6	144[a]		33.0[a]	18[a]		4.1			
	Female		Male		Female		Male		Female		Male	
	n	%	n	%	n	%	n	%	n	%	n	%
Age group distribution	176[b]	67.6	84[b]	32.3	114[b]	79.1	30[b]	20.8	6[b]	33.3	12[b]	66.6
					n		%					
U. urealyticum and *M. hominis* tests samples												
Urine sample					414		94.9					
Vaginal swab sample					22		5.0					
Infectious diseases					372[a]		85.3					
Gynecology and obstetrics					28[a]		6.4					
Requesting clinic												
Nephrology					8[a]		1.8					
Urology					8[a]		1.8					
Internal diseases					20[a]		4.5					
Patient complaints												
Urinary tract complaint infertility					414[a]		94.9					
					12[a]		5.0					

[a]:Ratio in all patients; [b]: Ratio among age groups

A total of 94.9% of the *U. urealyticum* and *M. hominis* tests were requested for patients with urinary complaints, and clinical requests were made for infectious diseases with a frequency of 85.3% (Table 1).

Growth occurred in 30.2% (132/436) of the patients. *U. urealyticum* was present in 28.8% (126/436) and *M. hominis* in 1.3% (6/436) of patients. *U. urealyticum* was positive in 80.3% (106/132) of females and 15.1% (20/132) of males. *U. urealyticum* was positive in 106 women, in two vaginal swabs and 104 urine samples; 62.2% of the women were young adults, and 37.7% were adults. Ninety percent of young adult males were positive, and 10% of adult males were positive (Table 2).

In our study, urine culture was requested for 288 patients simultaneously with all *Ureaplasma* and *Mycoplasma* requests. There was microorganism growth in 44.2% (92/208) of the urine cultures. *Escherichia coli, Proteus mirabilis, Candida albicans, Candida kefyr, Candida glabrata, Staphylococcus saprophyticus, Streptococcus agalactiae, Enterococcus faecium*, and *Staphylococcus aureus* were grown in urine cultures from patients. No microorganisms were grown in the urine cultures of 196 patients, and co-growth with *Mycoplasma* and *Ureaplasma* did not occur (Table 2).

Only 204 of all patients had both urinary leukocyte microscopy and leukocyte strip tests. Leukocyte microscopy and

Table 2. Features of the test all of patient

	MH and UU positivity in all patients				MH and UU positivity in age group											
					18–40				41–65				>65			
	Female		Male		Female		Male		Female		Male		Female		Male	
	Ureaplasma urealticum n=126[a] 28.8%															
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
U. urealyticum and *M. hominis* grown in all patient test samples n=132 (30.2%)	106[b]	80.3[a]	20[b]	15.1	66[b]	62.3	18[b]	90	40[b]	37.7	2[b]	10	0	0	0	0
	***Mycolasma hominis* n=6[a] 1.3%**															
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	4[b]	3.0	2[b]	1.5[a]	4[b]	66.6	0	0	0	0	4[b]	0	0	0	2	0

	Male		Female		Positivity in UU and MH growth test positivity		Negative in UU and MH growth test positivity	
	n	%	n	%	n	%	n	%
Urine culture n=288 (66.0%)	208[c]	72.2	80[c]	27.7	0	0	92[e]	44.2
Vagen culture n=24 (%5.3)	24	0	0	0	0	0	0	0
Urethral flow culture n=2	0	0	2	0	0	0	0	0
Amnion lıquıd culture n=2	2	0	0					
Urine microscopy leukocyte n=204 (46.7%)	146	71.5[d]	58	28.4	22[e]	16.6	54	17.7
Urinary leucocyte strip test n=204 (46.7%)	146	71.5[c]	0	28.4[c]	34	16.6	32	10.2

[a]: Ratio in all growth UU and MH; [b]: Ratio in self group; [c]: Ratio in all desired urine cultures; [d]: Ratio of positive in all of urine microskopy leucocyte tests; [e]: Other microorganisms grown in urine culture, *Escherichia coli, Proteus mirabilis, Albicans, Candida Kefyr, Candida glabrata, Staphylococcus saprophyticus, Streptococcus agalactia, Staphylococcus aureus, Enterococcus feacium, Staphylococcus aureus.* MH: Mycolasma hominisUU: Ureaplasma urealticum

leukocyte strip tests were requested for only 62 of the individuals with *Ureaplasma* and *Mycoplasma* (Table 2). A total of 35.4% (22/62) of urine microscopy results were positive, and 64.5% (40/62) were negative. On the other hand, the leukocyte strip test was positive for 54.8% (34/62) and negative for 45.1% (28/62) of patients. Urine leukocyte screening was low among all patients. Among these tests, urinary leukocyte screening was also low among patients with the growth of *U. urealyticum* and *M. hominis*. In addition, the rate of positivity of these tests in urine was low (Table 3).

Regarding antimicrobial susceptibility for U.urelyticum, the bacteria were greatly susceptible to pristinamycin (98.4%), minocycline (98.4%), josamycin, erythromycin, and roxithromycin (100%), tetracycline (92.0%), clarithromycin (96.8%), and levofloxacin (71.4%), whereas they were slightly susceptible to ciprofloxacin (6.3%), clindamycin (6.3%), and ofloxacin (15.8%) (Table 4).

M. hominis was observed among young adult women, whereas it was observed among men over 65 years of age. *M. hominis* was sensitive to pristinamycin, minocycline, josa-

Table 3. Urine microscopy and leukocyte strip test in samples with UU and MH growth

	UU and MH growth simultaneous request the test done		UU and MH positive in reproduction		UU and MH negative in growth	
	n	%	n	%	n	%
Urıne microscopy leukocyte n=124	62	30.3[a]	22	35.4[b]	40	64.5[b]
Urinary leucocyte strip test n=124	62	30.3[a]	34	54.8[b]	28	45.1[b]

[a]: Ratio in whole urine microscopy and urine strip test; [b]:Ratio between UU and MH negative or positive growth. UU: Ureaplasma urealticum; MH: Mycolasma hominis

mycin, and tetracycline (100%), roxithromycin and ofloxacin (66.6%), and erythromycin, clindamycin, ciprofloxacin, clarithromycin, and levofloxacin (33.3%) in the antimicrobial susceptibility test (Table 5).

DISCUSSION

U. urealyticum and *M. hominis* are members of the widely defined group of microorganisms of the genital tract. These bacteria cause infections with colonization in women, especially in the lower and upper genital tracts, and are responsible for acute urethritis, bacterial vaginitis, and PID; they also cause chorioamnionitis and adverse pregnancy outcomes in pregnant women and congenital pneumonia in fetuses and can be isolated from cerebrospinal fluid. These bacteria more rarely cause upper urinary tract infections and prostatitis in men.[5,6]

With the onset of sexual intercourse and throughout their reproductive years, women are exposed to many infectious agents, and the prevalence of *Mycoplasma* increases dramatically.[6–8] *Mycoplasma*, which is detected more frequently in women than in men, is highly dependent on the number of sexual partners and has been associated with different clinical conditions.[2,8] Some studies count *U. urealyticum* among sexually transmitted infections, and it is reported that it is more common among young adults, who are the most sexually active.[5,8]

Tüzemen et al.[9] reported that *Ureaplasma* and *Mycoplasma* reproduce more frequently in young adults: 54.81–46.83% among females and 42.8–38.10% among males, respectively. In a study conducted among 3410 patients, *U. urealyticum* was most common in the 20–29 age group (24.1%) and in the 30–39 age group (22.2%), mostly among females, with a rate of 24.4%.[10] In our study, the growth of *U. urealyticum* was 80.3–15.1% in males and females, respectively, and 63.6% (84/132) in the population aged 18–40 years, defined as the young adult group. In this age group, 62.2% (66/126) of *Ureaplasma* were found in females, 14.5% (18/126) in males, and only 1.3% (6/132). *Mycoplasma* was found, and while it was seen in 66.6% of females in this age group, there was no *Mycoplasma* growth in males (Table 2). These rates were similar to those among young adults and females in the literature. *Mycoplasma* growth was low in our study. The low growth of *Mycoplasma* may be the reason for examining the urine samples of the patient population presenting with urinary tract complaints.

There are many studies on the prevalence of these bacteria in our country and worldwide. In our country, Afacan et al.[11] found a combination of *Ureaplasma* and *Mycoplasma* in 150 (32.5%) of a total of 461 urine samples. *M. hominis* was present in 45 of these samples (9.8%), and *U. urealyticum* was present in 137 samples (29.7%); 32 samples (6.9%) had both microorganisms. Gözküçük et al.[12] detected *U. urealyticum* in 51 (38.9%) patients aged 18–42 years and *M. hominis* in 8 (6.1%) patients. Tüzemen et al.[9] examined a total of 2926 patients, 67.43% of whom were female and 32.57% of whom were male. A total of 1.23% of the patients were positive for *M. hominis* only, 22.25% for *U. urealyticum* only, and 3.79% for both. Ito et al.,[13] in their study, investigating the prevalence of gonococcal and nonchlamydial urethritis cases among men, found the prevalence of *M. hominis* to be 5.8%; they reported the prevalence as 19.5% for *U. urealyticum*. Baka et al.[14] defined *U. urealyticum* and *M. hominis* positivity as 52.6–3.3%, respectively, in their study among 157 female patients with chronic urinary tract complaints. In our study, growth occurred in 30.2% (132/436) of the patients. A total of 28.8% (126/436) of the patients had *U. urealyticum*, and 1.3% (6/436) had *M. hominis*. *U. urealyticum* and *M. hominis* positivity was observed in 35.4% (110/310) of females and 17.4% (22/126) of males (Table 2). The prevalence of these microorganisms in our study was similar to that in the literature.

Studies can increase the success of treatment according to the screening of the agents and antimicrobial results for these infections. When the samples and clinics where the tests were requested in this study were evaluated, 94.9% (414/436) were urine samples, and 5.0% (22/436) were vaginal swab samples (Table 2). Regarding the requesting clinics, 85.3% (372/436) of samples were from infectious disease clinics, 6.4% were from

Table 4. Antimicrobial susceptibility of *Ureaplasma urealyticum* by age and gender

Antimicrobial	Sensitivity	18–40				41–65				Total		Total		Total	
		Female n=6[a] 62.2%		Male n=18[b] 90%		Female n=40[a] 37.7%		Male n=2[a] 10%		Female (Total) n=106 84.1%[c]		Male (Total) n=20 15.8%[c]		n=126	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%
Pristinamycin	S	66	100	16	88.8	40	100	2	100	106	100	18	90	124	98.4
	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	R	0	0	2	11.1	0	0	0	0	0	0	2	10	4	1.5
Minocycline	S	66	100	16	88.8	40	100	2	100	106	100	18	90	124	98.4
	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	R	0	0	2	11.1	0	0	0	0	0	0	2	10	2	1.5
Josamycin	S	66	100	18	100	40	100	2	100	106	100	20	100	126	100
	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	R	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Erythromycin	S	66	100	6	88.8	40	100	2	100	106	100	8	30	126	100
	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	R	0	0	2	11.1	0	0	0	0	0	0	2	10	0	0
Roxithromycin	S	66	100	18	100	40	100	2	100	106	100	20	100	126	100
	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	R	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Clindamycin	S	0	0	6	37.5	2	5	0	0	2	1.8	6	33.3	8	6.3
	I	10	15.5	2	11.1	2	5	2	100	12	11.3	4	20	16	12.6
	R	56	84.8	10	62.5	36	90	0	0	92	86.7	10	50	102	80.9
Ofloxacin	S	10	15.5	6	33.3	2	5	2	100	12	11.3	8	40	20	15.8
	I	38	57.5	6	33.3	22	55	0	0	60	56.6	6	30	66	52.3
	R	18	27.2	6	33.3	16	40	0	0	34	32.0	6	30	40	31.7
Ciprofloxacin	S	4	6.0	4	22.2	0	0	0	0	4	3.7	4	20	8	6.3
	I	6	9.0	4	22.2	2	5	2	100	8	88.6	6	30	14	11.1
	R	56	84.5	10	55.5	38	95	0	0	94	7.5	10	50	104	82.5
Clarithromycin	S	62	93.9	18	100	40	100	2	100	102	96.2	20	100	122	96.8
	I	2	3.0	0	0	0	0	0	0	2	1.8	0	0	22	1.5
	R	2	3.0	0	0	0	0	0	0	2	1.8	0	0	2	1.5
Tetracycline	S	64	96.9	10	55.5	40	100	2	100	104	98.1	12	60	116	92.0
	I	0	0	4	22.2	0	0	0	0	0	0	4	20	4	3.1
	R	2	3.0	4	25	0	0	0	0	2	1.8	6	20	6	4.7
Levofloxacin	S	52	78.7	10	55.5	26	6.5	2	100	78	73.5	12	60	90	71.4
	I	10	15.5	4	22.2	0	0	0	0	10	94.3	4	20	14	11.1
	R	4	6.0	4	22.2	14	35	0	0	18	16.9	4	20	22	17.4

[a]: There was no reproduction in the ≥65 age group in all cultures of female patients where microorganisms grew; [b]: in all cultures of male patients where microorganisms grew; [c]: in all cultures of patients where microorganisms grew. S: Sensitive; I: Intermediate; R: Resistance

obstetrics and gynecology clinics, and only 1.8% (8/436) were from urology clinics (Table 1). Our hospital in Istanbul has 2648 beds and cares for 20,000 outpatients in 1 day, and 500 women receive infertility treatment every year. Considering that there are infertility treatments, such as *in vitro* fertilization, in gynecology and obstetrics clinics, neonatal clinics, urology

Table 5. Antimicrobial susceptibility of *M. hominis* by gender

Antimicrobial	Sensitivity	Female (n=4)		Male (n=2)		Total (n=6)	
		n	%	n	%	n	%
Pristinamycin	S	4	100	2	100	6	100
	I	0	0	0	0	0	0
	R	0	0	0	0	0	0
Minocycline	S	4	100	2	100	6	100
	I	0	0	0	0	0	0
	R	0	0	0	0	0	0
Josamycin	S	4	100	2	100	6	100
	I	0	0	0	0	0	0
	R	0	0	0	0	0	0
Erythromycin	S	2	50	0	0	2	33.3
	I	0	0	2	100	2	33.3
	R	2	50	0	0	2	33.3
Roxithromycin	S	2	50	2	100	4	66.6
	I	0	0	0	0	0	0
	R	2	50	0	0	2	33.3
Clindamycin	S	2	50	0	0	2	33.3
	I	0	0	0	0	0	0
	R	2	50	2	100	4	66.6
Ofloxacin	S	2	50	2	100	4	66.6
	I	2	50	0	0	2	33.3
	R	0	0	0	0	0	0
Ciprofloxacin	S	2	50	0	0	2	33.3
	I	0	0	2	100	2	33.3
	R	2	50	0	0	2	33.3
Clarithromycin	S	2	66.6	0	0	2	33.3
	I	0	0	2	100	2	33.3
	R	2	33.3	0	0	2	33.3
Tetracycline	S	4	100	2	100	6	100
	I	0	0	0	0	0	0
	R	0	0	0	0	0	0
Levofloxacin	S	2	50	0	0	2	33.3
	I	2	50	2	100	4	66.6
	R	0	0	0	0	0	0

S: Sensitive; I: Intermediate; R: Resistance

clinics, and intensive care units, it is thought-provoking that the number of materials requested in 1 year is low. Clinicians consider and research these factors as a last resort in the etiology of the disease. Among the reasons for this are the widespread colonization of *M. hominis* and *U. urealyticum* in the lower and upper genital tracts of healthy individuals. Studies explaining the relationship between these microorganisms and disease mostly focus on the lower urogenital system and ignore multifactorial disease factors. This approach causes clinicians to delay the diagnosis of these factors in the etiology of the disease.[4,15,16] However, there are practical and rapid test methods for the identification of these microorganisms. Evidence-based diagnosis and treatment without permanent damage to the patient are possible with early diagnosis. This suggests that there is a need to explain algorithms for diagnosing *Mycoplasma* and *Ureaplasma* to clinicians.

The simplest way to avoid therapeutic failures is through the application of rational treatment regimens. There are simple, commercially available systems by which *Ureaplasma* and *Mycoplasma* can be identified and antimicrobial susceptibility established *in vitro* that should be incorporated into routine laboratory procedures in every case. If the etiology is not related to urethral or bladder anatomical and/or functional anomalies, the microbiology laboratory can be of great help in the treatment of these patients. Rather than considering more invasive techniques, it is preferable to start with simple laboratory tests and cultures. Many physicians use tests that can show polymorphonuclear cells or bacteriuria in a urine sample without the need for culture.[5] These tests are characterized by good specificity; however, they have a rather low sensitivity. Pelit et al.[17] found leukocyte positivity for *U. urealyticum*, and *M. hominis* to be 33% and 20%, respectively, in their study titled Investigation of the Frequency of *Neisseria gonorrhoeae, Chlamydia trachomatis*, *U. urealyticum* and *M. hominis* in Male Patients with Urethritis Symptoms. When evaluated for both *U. urealyticum* and *M. hominis* that reproduced in our study, simultaneous urine strip tests and urine microscopy were found to be positive in 35.4–54.8% and negative in 64.5–45.1% of patients, respectively (Table 3). Our study suggested that although leukocyte positivity in the complete urine test showed that an infection was present, it was not always positive. Although leukocyte negativity in the complete urine test showed that there was no infection, it was thought that there might be an infection, and clinicians would be insufficient in the diagnosis and cause delays in the treatment.

The diagnosis of an infection caused by these bacteria is determined by the isolation of these microorganisms from the site of infection. However, the diagnosis of an infection caused by *Mycoplasma* or *Ureaplasma* is difficult. Because they are not usually isolated in pure culture, this makes evaluation even more difficult. If an etiological agent is not identified in the routine examination of a patient who previously presented with urinary tract complaints, these microorganisms should be considered.[18] However, it has been reported in the literature that these microorganisms may

be associated with infertility, have negative effects during pregnancy, affect the fetus, and cause infections such as prostatitis and urethritis in male patients.[4,5,14]

Empirical treatment of *Ureaplasma* and *Mycoplasma* without an antibiogram may be ineffective in their treatment and may lead to prolongation of treatments and unnecessary antimicrobial treatments. Although the frequency of infections associated with *U. urealyticum* and *M. hominis* may vary depending on community structure and changes, even from region to region, antibiotic susceptibility rates also differ from hospital to hospital depending on the previous use of antimicrobials.[1] Each center should contribute to effective treatment by creating its own up-to-date data.

Numerous antimicrobial test studies have been conducted on *U. urealyticum* in our country and worldwide. Tüzemen et al.,[9] in their research in 2015 and 2016, found sensitivity rates to tetracycline, ciprofloxacin, ofloxacin, levofloxacin, and clindamycin of 55.56%, 5.38%, 22.05%, 69.69%, and 5.38%, respectively. In Cameroon, Longdoh et al.[19] found *U. urealyticum* susceptible to tetracycline, levofloxacin, and ofloxacin (17.2%, 62.1%, and 3.5%, respectively) and not at all to ciprofloxacin or clindamycin. Kechagia et al.[20] found tetracycline, ciprofloxacin, and ofloxacin sensitivity rates of 87.4%, 4.5%, and 9.0%, respectively, in Greece; Zheng et al.[21] in China, in their study among 4280 Chinese patients, reported reduced sensitivity for azithromycin (24.45%), ofloxacin (20.13%), levofloxacin (8.56%), and ciprofloxacin (16.55%). In Poland, Kasprzykowska et al.[22] analyzed 12-year data on *Ureaplasma* and described a decrease in resistance to ofloxacin, erythromycin, and tetracycline.

In our study, tetracycline susceptibility was found to be 92.0–100%, 6.3–33.3% for ciprofloxacin, 6.3–33.3% for clindamycin, 15.8–66.6% for ofloxacin, and 71.4–33.3% for levofloxacin for *U. urealyticum* and *M. hominis*, respectively. *U. urealyticum* was found to be susceptible to pristinamycin (98.4%), minocycline (98.4%), josamycin (100%), and erythromycin (100%) (Tables 3, 5).

The sensitivity of resistance to tetracycline by encoding a protein that binds to the ribosome through the tet (M) determinant for tetracycline has been reported to reach 40–50%.[4] However, in our study, tetracycline was found to be quite sensitive, as in the study conducted in Greece. The increase in sensitivity may be due to the change in antibiotic use policies over time and the fact that the tetracycline group was not chosen as a priority in the empirical treatment of urinary infections due to the production of reproducing microorganisms in urine samples.

When the sensitivity rates between men and women were examined for *U. urealyticum* in our study, females were more sensitive to tetracycline at 98.1–60.0%. Females were less sensitive to clindamycin (1.8–33.3%), ciprofloxacin (3.7–20%), and ofloxacin (11.3–40%). When evaluated in terms of age groups, there was no difference (Table 3).

A few (only six) *M. hominis* isolates were fully susceptible (100%) to minocycline, pristinamycin, and josamycin, while susceptibility to other antimicrobial agents was mainly 'intermediate' or 'resistant' (Table 5).

CONCLUSION

As seen in our study, clinicians mostly request *Ureaplasma* and *Mycoplasma* tests for patients with chronic urinary complaints. For this reason, in our study, *Mycoplasma* and *Ureaplasma* were produced in the urine samples of patients who came to the infectious disease outpatient clinic with complaints of chronic urinary tract infections, and antimicrobial testing was performed. Antimicrobial susceptibility was then evaluated accordingly. The number of requested tests was low for reasons other than urinary complaints. According to the literature, these sexually transmitted microorganisms cause infections in men and women at young ages and can cause infertility. For this reason, it was expected that the number of tests requested from obstetrics or urology clinics would be higher. However, the test request was low. Clinicians should remember these microorganisms as disease agents and seek help from microbiology laboratories. Urine microscopy may not always guide the patient's diagnosis. Practical commercial kits are available that allow identification and antimicrobial testing of *U. urealyticum* and *M. hominis*. This information should be disseminated in laboratories and contribute to the diagnosis and treatment of the agent.

Disclosures

Ethics Committee Approval: The study was approved by the Başakşehir Çam and Sakura City Hospital Ethics Committee (No: KAEK/2021.11.246, Date: 17/11/2023).

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REFERENCES

1. Balows A. Manual of clinical microbiology. 8th ed. Murray PR, Baron EJ, Jorgenson JH, Pfaller MA, Yolken RH, editors. ASM Press; 2003. Diagn Microbiol Infect Dis 2003;47:625–6.
2. McCormack WM, Almeida PC, Bailey PE, Grady EM, Lee YH. Sexual activity and vaginal colonization with genital mycoplasmas. JAMA 1972;221:1375–7. [CrossRef]
3. Tuddenham S, Hamill MM, Ghanem KG. Diagnosis and treatment of sexually transmitted infections: a review. JAMA 2022;327:161–72. [CrossRef]
4. Waites KB, Katz B, Schelonka RL. Mycoplasmas and ureaplasmas as neonatal pathogens. Clin Microbiol Rev 2005;18:757–89. [CrossRef]
5. Soffer Y, Ron-El R, Golan A, Herman A, Caspi E, Samra Z. Male genital mycoplasmas and Chlamydia trachomatis culture: its relationship with accessory gland function, sperm quality, and autoimmunity. Fertil Steril 1990;53:331–6. [CrossRef]
6. Taylor-Robinson D, Furr PM. Update on sexually transmitted mycoplasmas. Lancet 1998;351(Suppl 3):12–5. [CrossRef]
7. Unemo M, Jensen JS. Antimicrobial-resistant sexually transmitted infections: gonorrhoea and *Mycoplasma* genitalium. Nat Rev Urol 2017;14:139–52. [CrossRef]
8. Murtha AP, Edwards JM. The role of *Mycoplasma* and *Ureaplasma* in adverse pregnancy outcomes. Obstet Gynecol Clin North Am 2014;41:615–27. [CrossRef]
9. Tüzemen NÜ, Efe K, Özakın C. *Mycoplasma hominis* and *Ureaplasma urealyticum*: their role in urogenital system infections and retrospective evaluation of antibiotic resistance rates. Klimik Derg [Article in Turkish] 2019;32:40–5. [CrossRef]
10. Beşli Y, Karatuna O, Akyar I. Evaluation of *in vitro* antimicrobial susceptibility in *Ureaplasma urealyticum* and *Mycoplasma hominis* strains isolated from genitourinary tract samples. ANKEM Derg [Article in Turkish] 2017;31:97–105. [CrossRef]
11. Afacan G, Yumuk Z, Yılmaz NÖ, Balıkçı E, Mercan F. The prevalence and antibiotic susceptibility of *Mycoplasma hominis* and *Ureaplasma urealyticum* in patients with sterile pyuria. ANKEM Derg [Article in Turkish] 2007;21:232–6.
12. Gözüküçük R, Çakıroğlu B, Çaşkurlu T. Pathogens in patients with urethral discharge and their antibiotic susceptibilities. New J Urol [Article in Turkish] 2012;7:8–11.
13. Ito S, Tsuchiya T, Yasuda M, Yokoi S, Nakano M, Deguchi T. Prevalence of genital mycoplasmas and ureaplasmas in men younger than 40 years-of-age with acute epididymitis. Int J Urol 2012;19:234–8. [CrossRef]
14. Baka S, Kouskouni E, Antonopoulou S, Sioutis D, Papakonstantinou M, Hassiakos D, et al. Prevalence of *Ureaplasma urealyticum* and *Mycoplasma hominis* in women with chronic urinary symptoms. Urology 2009;74:62–6. [CrossRef]
15. Horner P, Thomas B, Gilroy CB, Egger M, Taylor-Robinson D. Role of *Mycoplasma* genitalium and *Ureaplasma urealyticum* in acute and chronic nongonococcal urethritis. Clin Infect Dis 2001;32:995–1003.
16. Kilic D, Basar MM, Kaygusuz S, Yilmaz E, Basar H, Batislam E. Prevalence and treatment of Chlamydia trachomatis, *Ureaplasma urealyticum*, and *Mycoplasma hominis* in patients with non-gonococcal urethritis. Jpn J Infect Dis 2004;57:17–20.
17. Pelit S, Bulut ME, Bayraktar B. The frequency of *Neisseria gonorrhoeae, Chlamydia trachomatis, Ureaplasma urealyticum* and *Mycoplasma hominis* in patients with urethral symptoms. Med J Bakirkoy [Article in Turkish] 2017;13:10–3. [CrossRef]
18. Potts JM, Ward AM, Rackley RR. Association of chronic urinary symptoms in women and *Ureaplasma urealyticum*. Urology 2000;55:486–9.
19. Longdoh NA, Gregory HEE, Djeumako WA, Nguedia AJC, Francois-Xavier MK, Tebit KE. The occurrence and antimicrobial susceptibility patterns of *Mycoplasma hominis* and *Ureaplasma urealyticum* in pregnant women in three district hospitals in Douala, Cameroon. JAMMR 2018;27:1–11. [CrossRef]
20. Kechagia N, Bersimis S, Chatzipanagiotou S. Incidence and antimicrobial susceptibilities of genital mycoplasmas in outpatient women with clinical vaginitis in Athens, Greece. J Antimicrob Chemother 2008;62:122–5.
21. Zheng WW, Zhang WJ, Cui D, Nie ZC, Ding BS, Cheng JH, et al. Examination of *Ureaplasma urealyticum* and *Mycoplasma hominis* in 4082 Chinese patients. Braz J Med Biol Res 2020;54:e10099. [CrossRef]
22. Kasprzykowska U, Sobieszczańska B, Duda-Madej A, Secewicz A, Nowicka J, Gościniak G. A twelve-year retrospective analysis of prevalence and antimicrobial susceptibility patterns of *Ureaplasma* spp. and *Mycoplasma hominis* in the province of Lower Silesia in Poland. Eur J Obstet Gynecol Reprod Biol 2018;220:44–9. [CrossRef]