

Association of *Ureaplasma urealyticum* Colonization in Male Urethra and *Condyloma acuminatum*

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Abstract

Background: The frequent coexistence of two or more sexually transmitted diseases in one patient has been reported in non-dermatological literature, mostly in languages other than English. Identification of *Ureaplasma urealyticum*, *Chlamydia trachomatis* and *Mycoplasma hominis* in men with other STDs is important, since these bacteria have been implicated in a variety of diseases such as non-gonococcal urethritis, premature rupture of fetal membranes, and infertility in female sexual partners of these patients.

Objective: To assess the frequency of concomitant STD, particularly urethral colonization of *U. urealyticum*, *C. trachomatis* and *M. hominis*, in men consulting for suspected STD-related symptoms.

Methods: All patients attending our dermatology clinic for STD-related symptoms during a 12 month period in 1996–97 underwent systematic clinical and laboratory screening for syphilis, gonorrhoea, NGU, prostatitis, genital herpes simplex infection, *Condyloma acuminatum*, urethral carriage of *U. urealyticum*, *C. trachomatis* and *M. hominis*, as well as serological screening for HIV, and hepatitis B and C infections.

Results: A total of 169 men with STD-related symptoms were enrolled in the study. The following clinical diagnoses were established: NGU in 109 men, *C. acuminatum* in 40, genital herpes simplex in 10, prostatitis in 7, latent syphilis in 6, primary syphilis in 1, and Behcet's disease in 1. No clinical evidence of STD was found in 13 patients. Of the 169 patients, 39 (23%) had two or more concomitant STDs, of whom 27 (69%) had *C. acuminatum* associated with one or more of the urethral pathogens. A positive *U. urealyticum* culture was found in 67.5% (27/40) of the men with *C. acuminatum* as compared to 42% (40/96) among the patients with NGU who did not have *C. acuminatum* ($P=0.004$, χ^2 test). Conversely, the prevalence of *C. acuminatum* among patients positive for *U.*

urealyticum was significantly higher than the prevalence among those who were negative – 27/75 (36%) vs. 13/94 (14%), $P<0.0009$, χ^2 test. About half of the *U. urealyticum*-positive patients with *C. acuminatum* had no clinical signs or symptoms of urethritis.

Conclusion: Our findings suggest that patients with *C. acuminatum* should be assessed for *U. urealyticum* carriage and, when identified, their sexual contacts should be actively sought and treated.

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The coexistence of two or more sexually transmitted diseases was reported in non-dermatological literature, mostly in non-English languages [1–5]. Asymptomatic carriage of *U. urealyticum*, *C. trachomatis* and *M. hominis* merits particular attention, as its presence in the female genital tract is implicated in substantial perinatal and neonatal morbidity [6]. Considering the high risk of cross-infection among sexual partners, identification of *U. urealyticum* as a concomitant STD is of utmost importance in the management of these patients and their sexual contacts. The purpose of this study was to assess the frequency of concomitant STD in men consulting for suspected STD-related symptoms.

Methods

Patient population

Our dermatology clinic is located in the regional ambulatory health center of the Clalit Health Services, the largest health maintenance organization in the country. Patients have unlimited access to our clinic but are usually referred by their primary doctor. Of 32,000 annual visits to the clinic, all patients with suspected STD are examined by one dermato-venereologist (E.M.). Since women with STDs consult or are referred traditionally to a gynecologist, we expected a low proportion of females in our study population.

During the period June 1996 to July 1997 all patients consulting for suspected STD were systematically evaluated for coexistence of two or more STDs. Urethritis was defined as the presence of burning, stinging pain or

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STDs = sexually transmitted diseases

NGU = non-gonococcal urethritis

urethral discharge from the penile meatus. The diagnosis of prostatitis was made if palpation of the gland was painful and was associated with meatal discharge. The diagnoses of *Condyloma acuminatum*, genital herpes simplex virus infection, gonorrhoea and syphilis were established according to clinical features and appropriate laboratory tests. All patients were serologically screened for the presence of antibodies to *C. trachomatis*, *M. hominis*, *U. urealyticum*, HIV and syphilis. Urethral or cervical smears were obtained for direct examination for presence of gonococci as well as for *C. trachomatis*, *U. urealyticum* and *M. hominis* cultures.

Laboratory methods

Urethral culture specimens, inserted in 10B broth, were transported immediately to the laboratory and cultured within 1–2 hours [6]. The original specimens and tenfold serial dilution of the 10B broth were plated on A8 agar plates for quantitative determination of colony-forming units. CFU of all dilutions were determined after 3–4 days. *M. hominis* was cultured in a similar way in an arginine-containing medium. Culture procedure for *C. trachomatis* was performed according to standard procedure [7]. Antibodies to *U. urealyticum* and *M. hominis* in the sera were measured by enzyme-linked immunoabsorbent assay, as previously described [8]. Titers above 1:160 were considered positive.

Statistical analysis

Fisher's exact test, χ^2 test, and Student's *t*-test were performed using SPSS software.

Results

During the study period 173 patients were evaluated for suspected STD: 169 males and 4 females. Because of the expectedly low number of females in the study, they were excluded from statistical analyses. The mean age of the 169 males was 35 years (SD 11.75, range 17–71). All but one patient were heterosexual. The reason for referral was suspected urethritis in 113 patients (66.9%), genital warts in 25 (14.8%), genital ulcers or blisters in 11 (6.5%), and fear of contracting STD in 20 patients even though they had no symptoms.

After clinical examination, the following diagnoses were established: NGU in 109 men, prostatitis in 7, *C. acuminatum* in 40, genital herpes simplex virus in 10, primary syphilis in 1, gonorrhoea in 1, Behcet's disease in 1, and no clinical evidence of STD in 13 patients. Subsequent laboratory analyses led to the diagnosis of latent syphilis in six patients. Thirty-nine of the 169 patients (23%) had two concomitant STDs, of whom 13 (33%) had *C. acuminatum* associated with NGU. There were no cases of HIV infection in the study group.

Urethral cultures for *U. urealyticum*, *C. trachomatis* and *M. hominis* were positive in 75 (44%), 8 (4.7%) and 3

Table 1. Frequency of positive urethral cultures and smear for gonococci by clinical diagnosis

	<i>U.urealyticum</i> (n=75)	<i>C.trachomatis</i> (n=8)	<i>M.hominis</i> (n=3)	Gonorrhoea (n=0)
Urethritis (n=109)	53 [*] (49%)	6 ^{**} (5.5%)	2 (1.8%)	0
Prostatitis (n=7)	4 ^{***} (57%)	0	0	0
Condyloma (n=40)	27 [*] (67.5%)	2 ^{**} (5%)	1 (2.5%)	0
Syphilis (n=7)	0	0	0	0
No STD (n=13)	4 (11.6%)	1 (7.7%)	0	0
Genital herpes simplex virus (n=10)	1 (10%)	0	0	0

* 13 of these had concomitant *C.acuminatum* and urethritis

** 1 of these had concomitant *C.acuminatum* and urethritis

*** 1 of these had no symptoms of urethritis, yet on clinical examination the prostate was tender and its massage elicited *U. urealyticum*-culture positive discharge.

(1.8%) patients, respectively, with antibodies to these pathogens demonstrated in 15 (8.9%), 12 (7.1%) and 1 (0.6%) patients, respectively. Among the 109 men with clinical urethritis, only in 61 (56%) patients was an etiologic agent recovered in urethral cultures.

Among the 109 patients with clinically overt urethritis, *C. acuminatum* was found on the routine physical examination in 13 cases, whereas none of the men who referred for genital warts had clinical features of urethritis. *U. urealyticum* was recovered in urethral cultures from all 13 patients with clinical urethritis and *C. acuminatum*. In addition, *U. urealyticum* cultures were positive in 14 of the 27 men with *C. acuminatum* who did not have clinical urethritis. Overall, positive *U. urealyticum* cultures were found in 67.5% (27/40) of men with *C. acuminatum* as compared to 42% (40/96) among the patients with NGU who did not have *C. acuminatum* ($P=0.004$, χ^2 test). Conversely, the prevalence of *C. acuminatum* among patients positive for *U. urealyticum* was significantly higher than the prevalence among subjects who were negative – 27/75 (36%) vs. 13/94 (14%), $P<0.0009$, χ^2 test. In addition, *C. trachomatis* was recovered in two cultures and *M. hominis* in one culture of patients with *C. acuminatum*. Table 1 summarizes the distribution of positive laboratory analyses by clinical diagnosis.

There were no significant differences in age among patients with *C. acuminatum* or without (median 31 vs. 33 years, respectively; $P=0.50$, *t*-test) or between subsets of *C. acuminatum* patients with cultures positive for *U. urealyticum* versus those with negative cultures (median 28.5 vs. 35 years, respectively; $P=0.73$, *t*-test).

Discussion

In a previous study [9], colonization of *U. urealyticum* in male urethra in southern Israel was found in 36% of

CFU = colony-forming units

asymptomatic men and in 66% of men with non-gonococcal urethritis. In contrast to many other geographical areas where *C. trachomatis* is the most frequent urethral resident and pathogen, in our region it is found only in 1–3% of the general male population and in 13–25% of men with non-gonococcal urethritis [9,10]. In this study the prevalence of urethral cultures positive for both *U. urealyticum* and *C. trachomatis* among men with and without urethritis is comparable to the previous reports from our region. The search for concomitant STDs in men attending our venereology clinic has revealed a strikingly high frequency of *U. urealyticum* carriage among patients with *C. acuminatum*. In more than half of these patients there were no signs or symptoms of urethritis. Because of the small number of patients who had urethral cultures positive for both *C. trachomatis* and *M. hominis*, we could not explore whether carriage of these pathogens is associated with another STD.

It was previously reported that *U. urealyticum* antigens have a mitogenic effect on peripheral blood and synovial fluid macrophages in patients with Reiter's syndrome [9]. Possibly, this mitogenic effect plays a role in the high prevalence of *C. acuminatum* among *U. urealyticum*-positive patients. It is also possible that *U. urealyticum*-positive patients with *C. acuminatum* had some unrevealed risk factors for STDs, such as higher number of lifetime partners or different sexual habits. Regardless of this potential bias, these findings impose certain considerations.

The high proportion of married men among the subjects of the study suggests that a substantial number of the patients' spouses may acquire *U. urealyticum* from their husbands. Since it was previously shown that *U. urealyticum* carriage in the genital tract of pregnant women might be a risk factor for perinatal and neonatal morbidity, our findings suggest that fertile spouses of the patients are at considerable risk for perinatal complications. Although gynecological examination was strongly advised for sexual partners of all patients with a documented STD, the compliance with this recommendation could not be ascertained.

In conclusion, this study demonstrates a high prevalence of *U. urealyticum* infection among patients with *C. acuminatum*. Patients with *C. acuminatum* should be evaluated for carriage of *U. urealyticum* and, when identified, a search for carriage of this pathogen in their sexual contacts is warranted.

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*The things that will destroy us are:
politics without principle,
pleasure without conscience,
wealth without work,
knowledge without character,
business without morality,
science without humanity, and
worship without sacrifice.*

Anonymous