

# PREVALENCE OF UREAPLASMA UREALYTICUM, MYCOPLASMA HOMINIS AND HUMAN PAPILLOMAVIRUS COINFECTION IN PEOPLE ATTENDING A SEXUALLY TRANSMITTED INFECTIONS (STI)/HIV REFERENCE CENTRE IN SALVADOR, BAHIA, BRAZIL

## PREVALÊNCIA DA COINFEÇÃO POR UREAPLASMA UREALYTICUM, MYCOPLASMA HOMINIS E PAPILOMAVÍRUS HUMANO EM PESSOAS ATENDIDAS EM CENTRO DE REFERÊNCIA DE DOENÇAS SEXUALMENTE TRANSMISSÍVEIS (DST)/HIV EM SALVADOR, BAHIA

Alyce Lima Amorim<sup>1</sup> , Ana Gabriela Álvares Travassos<sup>1</sup> , Geovane Cruz de Souza<sup>1</sup> ,  
Vitor Cunha Fontes<sup>1</sup> , Maiara Timbó<sup>2</sup> , Eveline Xavier Souza<sup>2</sup> 

### ABSTRACT

**Introduction:** *Ureaplasma urealyticum* and *Mycoplasma hominis* are frequently found at many women's and men's urogenital tract, and have been associated with non-gonococcal urethritis, cervicitis, infertility, chorioamnionitis and adverse pregnancy outcomes. Some studies show high prevalence of *human papillomavirus* (HPV) in patients with non-gonococcal urethritis, while also presenting high frequency of *Ureaplasma urealyticum* infection in women with cervical cytology abnormalities and men with genital warts. **Objectives:** To evaluate the prevalence of *Ureaplasma urealyticum*, *Mycoplasma hominis* and HPV coinfection in people attending a sexually transmitted infections (STI)/HIV reference centre and to identify the risk factors associated. **Methods:** A cross-sectional study with patients aged >18 years, carried out for *Ureaplasma urealyticum* and *Mycoplasma hominis* from July 1<sup>st</sup> to December 31, 2015, in a STI/HIV reference centre from the State of Bahia, Brazil. Sociodemographic and clinical data were obtained from secondary data from patients' charts and laboratory findings, and analyzed using SPSS 20.0. Pearson's  $\chi^2$  test or Fisher's exact test was used to evaluate categorical variables. HPV clinical diagnosis was considered positive as the presence of genital warts. **Results:** In this study, 849 patients were included — 196 men and 653 women. Of the sample, 51.4% was diagnosed with at least one of the two bacteria. The prevalence of *Mycoplasma hominis* infection was higher in coinfection (16.7%) than in isolated infection (2.2%). The prevalence of *Ureaplasma urealyticum* isolated infection was 32.4%. A strong association was found between the presence of genital warts and *Ureaplasma urealyticum* infection, with an estimated risk of 1.230 ( $p=0.014$ ). **Conclusion:** Our findings suggest the need for further investigation for *Ureaplasma urealyticum* infection in patients presenting genital warts on physical examination. In addition, in this context, greater attention should be given to women and pregnant women.

**Keywords:** *Ureaplasma urealyticum*; *Mycoplasma hominis*; *Human papilloma virus*; reproductive tract infections.

### RESUMO

**Introdução:** *Ureaplasma urealyticum* e *Mycoplasma hominis* são frequentemente encontrados no trato urogenital de homens e mulheres, e têm sido associados à ocorrência de uretrites não gonocócicas, cervicite, infertilidade, corioamnionite e outras patologias obstétricas. Alguns estudos mostraram alta prevalência de papilomavírus humano (HPV) em pacientes com uretrites não gonocócicas, bem como alta frequência de infecção por *Ureaplasma urealyticum* em mulheres com anormalidades na citologia cervical e homens apresentando verruga genital. **Objetivos:** Avaliar a prevalência da coinfeção por *Ureaplasma urealyticum*, *Mycoplasma hominis* e HPV em pessoas atendidas em um centro de referência de DST/HIV e identificar os fatores de risco associados. **Métodos:** Estudo transversal com pacientes maiores de 18 anos, testados para *Ureaplasma urealyticum* e *Mycoplasma hominis* entre 1º de julho e 31 de dezembro de 2015, em um centro de referência de DST/HIV da Bahia, Brasil. Os dados clínicos e sociodemográficos foram obtidos por coleta de dados secundários a partir dos prontuários e achados laboratoriais dos pacientes e analisados usando SPSS 20.0. O teste de  $\chi^2$  Pearson ou teste exato de Fisher foram usados para avaliar as variáveis categóricas. O diagnóstico clínico do HPV foi considerado positivo quando houve presença de verruga genital. **Resultados:** Foram incluídos neste estudo, 849 pacientes, sendo 196 homens e 653 mulheres. Da amostra, 51,4% foi diagnosticada com infecção por pelo menos uma das duas bactérias. A prevalência de infecção por *Mycoplasma hominis* foi maior na coinfeção (16,7%) do que isoladamente (2,2%). A prevalência da infecção isolada por *Ureaplasma urealyticum* foi de 32,4%. Houve forte associação entre a presença de verruga genital e infecção por *Ureaplasma urealyticum*, com estimativa de risco de 1,230 ( $p=0,014$ ). **Conclusão:** Nossos achados sugerem a necessidade de investigação adicional para a infecção por *Ureaplasma urealyticum* nos pacientes apresentando verruga genital ao exame físico. Além disso, nesse contexto, maior atenção deve ser dada a mulheres e gestantes.

**Palavras-chave:** *Ureaplasma urealyticum*; *Mycoplasma hominis*; *Human papilloma virus*; infecções genitais.

## INTRODUCTON

*Ureaplasma urealyticum* (UU) and *Mycoplasma hominis* (MH), commonly known as mycoplasma and ureaplasma, are often isolated in the urogenital tract of men and women<sup>(1)</sup>. Simultaneous colonization by the two pathogens is very common and may be associated

with factors such as young age, low socioeconomic status, sexual relations with multiple partners, non-use of condoms and being afrodescendant<sup>(2)</sup>.

UU and MH have been associated with non-gonococcal urethritis, pelvic inflammatory disease, salpingitis, bacterial vaginosis, infertility, obstetric pathologies (premature delivery, abortion, postpartum and post-abortion fever, and chorioamnionitis) and pyelonephritis<sup>(2,3)</sup>. However, one of the main difficulties in identifying these organisms as causing these diseases is their occurrence in apparently healthy individuals<sup>(3)</sup>.

<sup>1</sup>Medical Course, Department of Life Sciences, Universidade Estadual da Bahia – Salvador (BA), Brazil.

<sup>2</sup>Medical Course, Universidade Federal da Bahia – Salvador (BA), Brazil.

*Human papillomavirus* (HPV) infection is a determining element in the development of most cases of cervical cancer in women, and has also been identified as a risk factor for the development of cancers of the penis, anus and oropharynx<sup>(4)</sup>. Genital HPV infection is usually transmitted during intercourse, and its prevalence in sexually active women worldwide can range from 20 to 60%, which allows us to conclude that this is one of the most common sexually transmitted infections (STIs) in women<sup>(5)</sup>.

The diagnosis of HPV may be clinical, determined by the presence of condyloma acuminatum or warts in the anogenital region; subclinical through examination of the affected region; pathological, by performing biopsy of the lesion; and, finally, diagnosis of latent (asymptomatic) form, obtained by molecular biology methods (polymerase chain reaction (PCR), hybrid capture)<sup>(6)</sup>.

Studies have shown a high prevalence of HPV in patients with gonococcal and non-gonococcal urethritis<sup>(7-10)</sup>. This may be associated with the fact that patients with urethritis represent a group of high-risk behaviors for STIs, including HPV infection<sup>(11)</sup>. In addition, the inflammation of the urinary tract shown in uncontrolled urethritis can induce cell exfoliation, which contributes to the detection of asymptomatic HPV infection in men<sup>(12)</sup>.

A study conducted in 2011 showed that women with abnormalities in the cytopathological examination of the cervix have a high frequency of UU and MH infections<sup>(7)</sup>. In this study, it was found that patients infected with these species have a risk of evolution of HPV infection increased by 4.7 times. In addition, a study conducted in Poland showed that 88.9% of women diagnosed with HPV in cytopathology had UU coinfection<sup>(13)</sup>.

A study evaluating the presence of STIs in male patients with condyloma acuminatum deserves attention, because it identified a prevalence of asymptomatic infection by UU in 67.5% of men who presented condyloma acuminatum<sup>(14)</sup>.

In view of the importance of diagnosing and treating symptomatic and asymptomatic infections by these microorganisms to ensure the interruption of the transmission cycle among the population, it was necessary to study the prevalence of these infections and the associated risk factors, with the intention of tracing a current epidemiological profile that may guide an update in the screening and management strategies of patients.

## OBJECTIVE

The main objective of this study was to evaluate the prevalence of UU, MH and HPV, coinfection and the presence of condyloma acuminatum in people treated at an STIs/HIV referral center in Salvador, Bahia. The secondary objective of the study was the determination of risk factors associated with the higher prevalence of these coinfections.

## METHODS

A cross-sectional study was performed with patients tested for UU and MH, between July 1<sup>st</sup> and December 31, 2015, through a retrospective analysis with secondary data from medical records and laboratory data. The data surveyed were recorded in a previously established form containing clinical and sociodemographic information.

All patients admitted and tested at the unit for UU and MH in the mentioned period were included. Exclusion criteria were age below 18 years and incomplete data regarding the study objective. Clinical and epidemiological data associated with the presence of UU and MH infection were evaluated in the medical records of patients seen at the Specialized Center for Diagnosis, Care and Research (*Centro Estadual Especializado em Diagnóstico, Assistência e Pesquisa — CEDAP*), in Salvador, Bahia.

The acquisition of biological material for the culture of MH and UU is done by collecting a sterile vial containing the first urinary jet in men and endocervical/vaginal material with brush or cytology brush in women. Screening, quantification and detection of antibiotic sensitivity were determined with the MYCOFAST Screening Evolution 3 kit, which presents sensitivity of 92.3% and specificity of 98.25% for UU, and sensitivity of 93.25% and specificity of 95.3% for MH. Infection by UU and/or MH was considered positive by positive culture result for one or both pathogens.

For the population studied, continuous quantitative variables (age) and nominal qualitative variables (gender, marital status, current pregnancy, contraceptive use, use of current condom, symptomatology, and presence of other STIs, including HPV) were adopted. The clinical and physical examination data of the patient were collected from the anamnesis performed on the day of collection of biological material for culture. HPV infection was considered positive when there was the presence of condyloma acuminatum (genital wart), recorded in medical records by the attending physician.

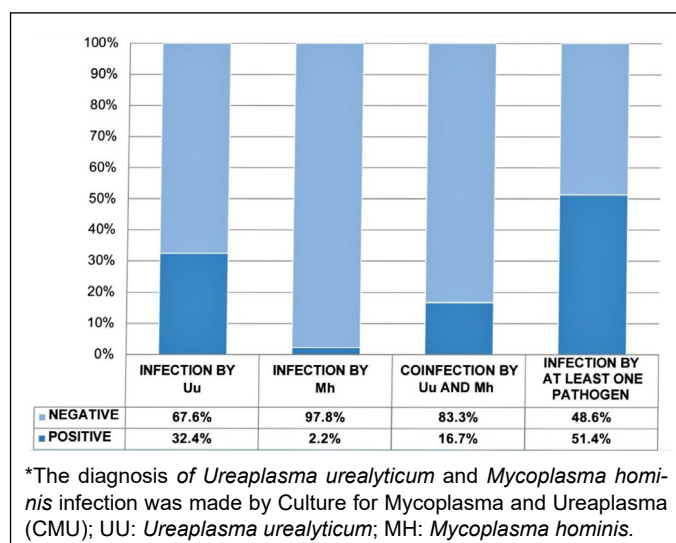
Subsequently, the data were entered in EPIDATA version 3.1 and compiled into a database with the Microsoft Excel 2017 program<sup>®</sup>. The analysis was performed with the program SPSS for Windows version 20.0<sup>®</sup>. Pearson  $\chi^2$  test or Fisher's exact test was used to evaluate categorical variables. The continuous variables were evaluated using Student's *t*-test. For all tests used, statistical significance is considered when the  $p < 0.05$  and 95% confidence interval (95%CI).

As this is a retrospective study, through a review of secondary data recorded in medical records and laboratory protocol book, with no interview, procedures or interventions, the study brings few risks to patients. The study was approved by the research ethics committee (CEP) of the Health Department of the State of Bahia (*Secretaria da Saúde do Estado da Bahia — SESAB*), through opinion number 1,792,012. Confidentiality will be maintained regarding the name and personal data obtained in the review of medical records as provided for in Resolution no. 466/2012.

## RESULTS

A total of 893 patients performed culture for MH and UU (CMU) between July and December 2015 at the studied STI/HIV reference center. Of this total, 44 patients were excluded from the sample, resulting in 849 patients included in the following analysis, among them 196 men and 653 women. The mean age among women was 35.17 years and, among men, 32.18 years, both with standard deviation of 11.38 years.

**Figure 1** shows the prevalence of UU and MH infection alone or together in the population studied. It is noted that more than half



**Figure 1** – Prevalence of *Ureaplasma urealyticum* and *Mycoplasma hominis* infections in patients treated at the sexually transmitted infections (STI)/human immunodeficiency virus (HIV) referral center, Salvador, Bahia, in 2015 (n=849).

of the population that underwent the ureaplasma and mycoplasma culture (UMC) was diagnosed with infection by at least one of the two bacteria (51.4%). The prevalence of MH infection was higher in coinfection (16.7%) than isolation (2.2%), reinforcing the synergism between simultaneous infection by the two bacteria. The prevalence of UU isolation infection (32.4%) exceeded more 30% of the prevalence of MH-isolated infection (2.2%).

**Table 1** shows that 89.7% of patients diagnosed with infection by at least one of the two bacteria were women. In addition, females had a 1,414 (95%CI 1.305–1.531) higher risk of UU and/or MH infection compared to males, which was statistically significant ( $p < 0.001$ ). Having a fixed partner was identified as a protective factor for UU and/or MH infection, with a 0.656 (95%CI 0.490–0.878) lower risk of having infection by at least one of the bacteria compared to patients without a fixed partner. This finding was statistically significant ( $p = 0.004$ ).

Also in **Table 1**, it is verified that 38.3% of patients diagnosed with infection by at least one of the bacteria have HIV, but this condition did not have a statistically significant association with the presence of UU and/or MH infection. The same occurred with the use of condoms; although there is no statistically significant association with the presence of infection by bacteria, a high prevalence of irregular use or no condom use was observed in the population diagnosed with UU and/or MH infection (51.8%).

Analyzing only the group of women who underwent UMC in the period studied, it was found that being pregnant presented a 3.159 (95%CI 1.419–7.033) higher risk of UU and/or MH infection, an alarming risk estimate that was statistically significant ( $p = 0.003$ ).

Starting from **Table 2**, the same phenomenon was verified within the group of patients who were diagnosed with condyloma acuminatum in the genital region on physical examination: the vast majority

**Table 1** – Prevalence of *Ureaplasma urealyticum* and/or *Mycoplasma hominis* infections according to sex, steady partner, human immunodeficiency virus (HIV) serological status, and condom use in patients treated at the sexually transmitted infections (STI)/HIV reference center, Salvador, Bahia (2015).

Categories	Infection by UU and MH				P-value ( $\chi^2$ )	OR (95%CI)
	Positive		Negative			
	Total=436	Total=413	Total=436	Total=413		
	n	%	n	%		
<b>Gender</b>						
Male	45	10.3	151	36.6	<0.001	0.282 (0.208–0.383)
Female	391	89.7	262	63.4		1.414 (1.305–1.531)
<b>Steady partner</b>						
Yes	63	14.4	91	22	0.004	0.656 (0.490–0.878)
No	373	85.6	322	78		1.097 (1.029–1.70)
<b>Serological status</b>						
HIV+	167	38.3	137	33.2	0.119	1.155 (0.963–1.384)
HIV-	269	61.7	276	66.8		0.923 (0.835–1.021)
<b>Use of condom</b>						
Regular	91	20.9	69	1.7	0.393	1.123 (0.860–1.468)
Irregular/None	226	51.8	201	48.7		0.958 (0.868–1.057)
<b>Pregnant*</b>						
Yes	33	8.4	7	2.7	0.003	3.159 (1.419–7.033)
No	358	91.6	255	97.3		0.941 (0.907–0.975)

\*Male patients were excluded for analysis of this variable; OR: odds ratio; 95%CI: 95% confidence interval; Pearson  $\chi^2$  test and Fisher's exact test were used for variable analysis; The diagnosis of *Ureaplasma urealyticum* and *Mycoplasma hominis* infection was made by Culture for Mycoplasma and Ureaplasma (CMU); UU: *Ureaplasma urealyticum*; MH: *Mycoplasma hominis*.

were female, representing 91.7% of patients with genital wart in the sample studied. Additionally, the female gender was identified with a higher risk 1.247 (95%CI 1.169–1.330) of presenting genital wart compared to males, a finding that was statistically significant ( $p < 0.001$ ).

Although most patients with genital wart did not have a fixed partner (86%), this factor did not present any statistically significant association with the presence of genital wart.

Also in **Table 2**, HIV+ serological status showed a lower association, with a risk of 0.344 (95%CI 0.231–0.512) lower than having genital wart when compared to the non-HIV-infected group; a finding that was statistically significant ( $p < 0.001$ ).

**Table 2** – Prevalence of condyloma acuminatum according to sex, steady partner, serological status for human immunodeficiency virus (HIV), condom use and pregnancy in patients treated at the sexually transmitted infections (STI)/HIV referral center, Salvador, Bahia (2015).

Categories	Condyloma acuminatum				P-value ( $\chi^2$ )	OR (95%CI)
	Positive		Negative			
	Total=157	Total=692	Total=157	Total=692		
	n	%	n	%		
Gender						
Male	13	8.3	183	26.4	<0.001	0.313 (0.183–0.535)
Female	144	91.7	509	73.6		1.247 (1.169–1.330)
Steady Partner						
Yes	22	14	132	19.1	0.137	0.735 (0.484–1.114)
No	135	86	560	80.9		1.063 (0.988–1.143)
Serological Status						
HIV+	22	14	282	40.8	<0.001	0.344 (0.231–0.512)
HIV-	135	86	410	59.2		1.451 (1.329–1.585)
Use of condom						
Regular	22	14	138	19.9	0.022	0.640 (0.429–0.957)
Irregular/ None	95	60.5	332	48		1.149 (1.035–1.277)
Pregnant*						
	n=144		n=509			
Yes	14	9.7	26	5.1	0.041	1.903 (1.021–3.548)
No	130	90.3	483	94.9		0.951 (0.898–0.995)

\*Male patients were excluded for analysis of this variable; Pearson  $\chi^2$  test and Fisher's exact test were used to analyze the variables; OR: odds ratio; 95%CI: 95% confidence interval.

The prevalence of irregular use or no condom use was high within the group of patients diagnosed with genital wart, representing 60.5% of these patients. Similarly, this behavior was identified as a risk factor for presenting genital wart, with an estimated risk 1.149 (95%CI 1.035–1.277) times higher than the group in regular condom use. This result was statistically significant ( $p=0.022$ ) to the  $\chi^2$  test.

Finally, **Table 2** also exposes another statistically significant finding ( $p=0.041$ ) that deserves attention: being pregnant was also identified as a risk factor for genital wart, with a risk of 1.903 (95%CI 1.021–3.548) higher than pregnant women presenting condyloma acuminatum in relation to the group of non-pregnant women.

**Table 3** shows the prevalence of symptoms within the population studied. In the group of patients diagnosed with infection by at least one bacteria (UU and/or MH), almost half (42.7%) did not show symptoms at the time of diagnosis. Among the symptoms

**Table 3** – Presence or not of symptoms according to positive or negative result for *Ureaplasma urealyticum* and/or *Mycoplasma hominis* infection in patients treated at the sexually transmitted infections (STI)/human immunodeficiency virus (HIV) reference center, Salvador, Bahia (2015).

Symptoms	Infection by UU and/or MH				P-value ( $\chi^2$ )	OR (95%CI)
	Positive		Negative			
	Total=436	Total=413	Total=436	Total=413		
	n	%	n	%		
Asymptomatic						
Yes	186	42.7	147	35.6	0.035	1.199 (1.012–1.420)
No	250	57.3	266	64.4		0.890 (0.799–0.992)
Genital pruritus						
Yes	34	7.8	23	5.6	0.195	1.400 (0.839–2.336)
No	402	92.2	390	94.4		0.976 (0.942–1.012)
Urethral discharge						
Yes	21	4.8	79	19.1	<0.001	0.252 (0.159–0.400)
No	415	95.2	334	80.9		1.177 (1.118–1.239)
Pelvic pain						
Yes	43	9.9	31	7.5	0.224	1.314 (0.845–2.044)
No	393	90.1	382	92.5		0.975 (0.935–1.016)
Dysuria						
Yes	30	6.9	96	23.2	<0.001	0.296 (0.201–0.436)
No	406	93.1	317	76.8		1.213 (1.144–1.287)
Hematuria						
Yes	0	0	2	0.5	0.236	1.005 (0.998–1.012)
No	436	100	411	99.5		
Pain in intercourse						
Yes	13	3	11	2.7	0.780	1.119 (0.507–2.471)
No	423	97	402	97.3		0.997 (0.974–1.020)
Vaginal discharge* n=391 n=262						
Yes	96	24.6%	65	24.8%	0.941	0.990 (0.753–1.301)
No	295	75.4%	197	75.2%		1.003 (0.917–1.098)

\*Male patients were excluded for analysis of this variable; Pearson  $\chi^2$  test and Fisher's exact test were used for variable analysis; the diagnosis of *Ureaplasma urealyticum* and *Mycoplasma hominis* infection was made by Culture for Mycoplasma and Ureaplasma (CMU); UU: *Ureaplasma urealyticum*; MH: *Mycoplasma hominis*; OR: odds ratio; 95%CI: 95% confidence interval.

contemplated by the study questionnaire, the most prevalent among patients with positive UMC results were: pelvic pain (9.9%), genital pruritus (7.8%), dysuria (6.9%) and urethral discharge (4.8%). Excluding male patients from the analysis, a high prevalence of vaginal discharge was found in female patients diagnosed with infection by at least one bacterium (24.6%).

The percentage of patients with urethral discharge and dysuria was higher in the group that was not diagnosed with either bacterium, representing 19.1 and 23.2% of the patients in this group, respectively. Thus, the presence of these two symptoms may be more associated with urogenital tract infections by other pathogens, which not UU and MH. This possibility is reinforced by the finding that the presence of urethral discharge and dysuria are protective factors for UU and/or MH infection, with a statistically significant  $p$  ( $p < 0.001$ ), speaking more in favor of other infections that need to be further investigated.

Finally, **Table 4** presents the statistical analysis of coinfection with UU, MH and HPV, the central objective of the present study. Of the total number of patients who had a clinical diagnosis of HPV ( $n=157$ ), 91 patients were identified with simultaneous UU infection, which represents more than half of the patients with genital wart (58%). In addition, UU infection was identified as a factor associated with the presence of genital wart, with an estimated risk of 1.230 (95%CI 1.054–1.436). This result presents statistical significance ( $p=0.014$ ). It is also observed in **Table 4** that, although almost a quarter of patients with condyloma acuminatum present MH infection simultaneously (22.9%), no statistically significant association was found between the presence of MH infection and the higher risk of developing genital wart.

**Table 4** – Prevalence of *Ureaplasma urealyticum* and *Mycoplasma hominis* infections in patients diagnosed with condyloma acuminatum at the time of collection of material for culture for mycoplasma and ureaplasma at the sexually transmitted infections (STI)/human immunodeficiency virus (HIV) reference center, Salvador, Bahia (2015).

RESULT CMU	Condyloma acuminatum				P-value ( $\chi^2$ )	OR (95%CI)
	Positive		Negative			
	Total=157 n	Total=692 %	Total=692 n	Total=157 %		
Infection by UU						
Yes	91	58.0	326	47.1	0.014	1.230 (1.054–1.436)
No	66	42.0	366	52.9		0.795 (0.653–0.968)
Infection by MH						
Yes	36	22.9	125	18.10	0.160	1.269 (0.915–1.762)
No	121	77.1	567	81.90		0.941 (0.858–1.031)

Pearson  $\chi^2$  test and Fisher's exact test were used for variable analysis; the diagnosis of *Ureaplasma urealyticum* and *Mycoplasma hominis* infection was made by Culture for Mycoplasma and Ureaplasma (CMU); UU: *Ureaplasma urealyticum*; MH: *Mycoplasma hominis*; OR: odds ratio; 95%CI: 95% confidence interval.

## DISCUSSION

In our study, the female gender was more associated with both UU and/or MH infection ( $p < 0.001$ ), and with the presence of condyloma acuminatum ( $p < 0.001$ ), indicating that being a woman in our sample was a risk factor for the presence of the STIS evaluated. Several factors may be associated with this finding. The position of the individual in society results from the interaction between different categories, often resulting from biological attributes that express a condition of inequality in the social space and determine the “social place” of each individual. Gender corresponds to one of these categories and, historically, gender inequality has determined a greater vulnerability of women in the social space, where the rights of access to services, including the health service, took a long time to achieve and still shows weaknesses<sup>(15)</sup>. The inequity of access of the female population, as well as the inferior role of women in sexual and reproductive decisions, typical of a patriarchal society that still characterizes contemporary Brazil<sup>(16,17)</sup>, have a direct impact on the greater vulnerability of women in the acquisition of STIs.

A finding deserves to be highlighted in the study: more than half of the participants (51.4%) was diagnosed with at least one of the two bacteria analyzed, and, of the total number of patients diagnosed with UU and/or MH, almost half (42.7%) presented no symptoms at the time of the consultation. This result is not unexpected. Many studies show the large number of asymptomatic patients who are diagnosed with infection by these bacteria, with the prevalence of ureaplasmas infection ranging from 40 to 80%, and mycoplasmas from 10 to 20% in women of asymptomatic reproductive age<sup>(9,18,19)</sup>. Mycoplasmas may be normal in inhabitants of the urogenital tract of man and woman in certain circumstances, but titration greater than or equal to  $10^3$  colony forming units (CFU)/mL already demonstrates imbalance of the microbiota and favors proliferation of other pathogens<sup>(20,21)</sup>. This leads to an important reflection about the strategies that need to be developed in order to identify the asymptomatic population with the infection through an expanded screening, so that they are treated properly, thus interrupting the transmission cycle.

Infection by MH leads to an increase in pH in the vaginal microenvironment, resulting from the production of ammonia from the breakdown of arginine, the largest source of mycoplasmas energy. Similarly, urease released by ureaplasmas hydrolyzes urea into ammonia and alkalizes the vaginal pH. This increase in pH is responsible for facilitating the development of aerobic vaginitis and bacterial vaginosis<sup>(20,21)</sup>. The combination of all these disorders to the vaginal microbiota increases the risks of complications during pregnancy, such as preterm delivery, abortion, corioamnionitis and even fetal funitis<sup>(19,22)</sup>. In our study, pregnancy was identified as a risk factor for the presence of UU and MH infection, as well as for the presence of genital wart. It is worth noting the risk of the presence of UU and/or MH infection in the group of pregnant women, which was 3.159 ( $p=0.003$ ) higher in relation to the group of non-pregnant women, indicating the need for greater commitment to clinical suspicion and diagnostic investigation of these infections during pregnancy in order to protect the pregnancy from possible complications.

As expected, the positive association between the presence of genital wart and UU infection was identified through this study, with

an estimated risk of 1,230 higher than patients not diagnosed with infection by the bacterium. In our study, the percentage of patients who presented condyloma acuminatum on physical examination, and simultaneously, were diagnosed with UU was of 58%; an alarming rate. A previous study, conducted with men at a Dermatological Institute in Israel, identified a high frequency of UU infection in patients with condyloma acuminatum identified on physical examination: more than half of patients with genital wart (67.5%) was diagnosed with UU infection, even without signs and symptoms of urethritis<sup>(14)</sup>. Another study, conducted with non-pregnant women in the Department of Gynecology of the University of Rome, determined that 53% of patients diagnosed with HPV infection by means of PCR also had UU infection detected through culture, with an estimated risk of 2.95 ( $p < 0.001$ )<sup>(23)</sup>.

Although the association between HPV infection and UU has been identified in some studies, it is not known exactly whether there is a synergism mechanism between these two pathogens. A mitogenic potential was attributed to UU antigens in a previous study conducted with patients with Reiter syndrome<sup>(24)</sup>. This knowledge allows us to possibly infer that UU has some role in stimulating cell proliferation evidenced in the form of condyloma acuminatum as a result of HPV infection.

However, the possibility that the association between the two pathogens is behavioral cannot be ruled out, since both are transmitted during intercourse, thus involving the same risk factors related to sexual habits<sup>(11,14)</sup>.

Despite the fact we did not find a statistically significant association between the presence of condyloma and MH infection, it was possible to identify a positive association between the presence of condyloma and UU infection, an alarming prevalence of at least one of the two bacteria investigated (51.4%) and high prevalence of UU and MH coinfection (16.7%) in the population studied. Attention should be paid to the fact that this research was conducted with a convenience sample and, therefore, the information cannot be extrapolated precisely to the general population. In a reference center for STIs, patients seeking care are expected to have coinfections.

## CONCLUSION

The identification of women and pregnant women as a group of greater vulnerability in the present study is an important factor that signals the need for actions that aim at expanding access to health information and care by this group, as well as encouraging female self-care by the health professional.

In health services, the research of mycoplasma and ureaplasma through the realization of culture is often neglected, even in the presence of symptoms of urethritis. The high prevalence found in this study, however, shows the need for change in this approach, so that the presence of genital wart may be another sign that these infections may be present.

As stated, this study was conducted with a convenience sample from a reference center specialized in the management of STIs, which determines some limitations. Therefore, it is essential to conduct research from diverse populations with broader characteristics, such as people assisted in primary care in Basic Health Units and Family Health Program.

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## Participation of each author

Ana Gabriela: definition of the methodology, statistical analysis of the data, and continuous guidance during writing of the work. Alyce Lima: data collection, database typing, statistical data analysis, table and chart construction, and job writing. Geovane Souza: data collection and database typing. Vitor Cunha: data collection and database typing. Maiara Timbó: definition of methodology, data collection, and statistical analysis of data. Eveline Xavier: definition of methodology, data collection, and statistical analysis of data.

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## Conflict of interests

There is no conflict of interest to be reported.

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**Address for correspondence:****ALYCE LIMA AMORIM**Rua Silveira Martins, 552, bloco 25, casa 4 – Cabula  
Salvador (BA), Brazil

CEP: 41150-000

E-mail: alyce\_amorim@hotmail.com

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