Antibiotic Susceptibility and Sequence Type Distribution of Ureaplasma Species Isolated from Genital Samples in Switzerland

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Antibiotic resistance in Ureaplasma urealyticum/Ureaplasma parvum and Mycoplasma hominis is an issue of increasing importance. However, data regarding the susceptibility and, more importantly, the clonality of these organisms are limited. We analyzed 140 genital samples obtained in Bern, Switzerland, in 2014. Identification and antimicrobial susceptibility tests were performed by using the Mycoplasma IST 2 kit and sequencing of 16S rRNA genes. MICs for ciprofloxacin and azithromycin were obtained in broth microdilution assays. Clonality was analyzed with PCR-based subtyping and multilocus sequence typing (MLST), whereas quinolone resistance and macrolide resistance were studied by sequencing gyrA, gyrB, parC, and parE genes, as well as 23S rRNA genes and genes encoding L4/L22 ribosomal proteins. A total of 103 samples were confirmed as positive for U. urealyticum/U. parvum, whereas 21 were positive for both U. urealyticum/U. parvum and M. hominis. According to the IST 2 kit, the rates of nonsusceptibility were highest for ciprofloxacin (19.4%) and ofloxacin (9.7%), whereas low rates were observed for clarithromycin (4.9%), erythromycin (1.9%), and azithromycin (1%). However, inconsistent results between microdilution and IST 2 kit assays were recorded. Various sequence types (STs) observed previously in China (ST1, ST2, ST4, ST9, ST22, and ST47), as well as eight novel lineages, were detected. Only some quinolone-resistant isolates had amino acid substitutions in ParC (Ser83Leu in U. parvum of serovar 6) and ParE (Val417Thr in U. parvum of serovar 1 and the novel Thr417Val substitution in U. urealyticum). Isolates with mutations in 23S rRNA or substitutions in L4/L22 were not detected. This is the first study analyzing the susceptibility of U. urealyticum/U. parvum isolates in Switzerland and the clonality outside China. Resistance rates were low compared to those in other countries. We hypothesize that some hyperendemic STs spread worldwide via sexual intercourse. Large combined microbiological and clinical studies should address this important issue.

Ureaplasma urealyticum, Ureaplasma parvum, and Mycoplasma hominis are causative agents of urogenital tract infections such as nonchlamydial and nongonococcal urethritis, prostatitis, cervicitis, and pelvic inflammatory disease. Associations with adverse pregnancy outcomes, including miscarriage, chorioamnionitis, and preterm birth, as well as postpartum lung disease, bacteremia, and meningitis in newborns and fatal hyperammonemia in adults, have also been suggested. U. urealyticum and M. hominis are members of the Mycoplasmataceae family and the Mollicutes class and are characterized by lack of a cell wall, small genome size, and limited biosynthetic functions. U. urealyticum was previously divided into biovar 1 and biovar 2, which, based on molecular analyses, are now known to constitute the U. urealyticum and U. parvum species, belonging to 14 serovars. Together with other Mycoplasmataceae members, U. urealyticum, U. parvum, which includes serovars 1, 3, 6, and 14, and M. hominis are generally referred to as “genital mycoplasmas.”

In China, 55% of samples were female outpatients with various genital manifestations tested positive for Ureaplasma spp. and/or M. hominis; in the same setting, the prevalence of U. urealyticum was higher than the prevalence of M. hominis in single infections and coinfections (31.2% versus 0.7% and 31.2% versus 1.9%, respectively). In an Italian study, 19% of endocervical, urethral, or vaginal swabs from adult outpatients tested positive for genital mycoplasmas. In a prospective cohort survey from the United States, almost one-half of preterm infants were positive for Ureaplasma spp. in one or more compartments (i.e., respiratory tract, blood, and/or cerebrospinal fluid). A recent analysis from South Africa detected Ureaplasma spp. in 76% of pregnant women; 40% of them were coinfected/colonized with M. hominis. Overall, most of the published studies comparing adverse pregnancy outcomes showed significant associations with the presence of U. urealyticum or M. hominis.

Due to the lack of peptidoglycan, Ureaplasma spp. and Mycoplasma spp. are naturally resistant to β-lactams, whereas sulfonamides and trimethoprim are inactive because of the absence of folic acid synthesis. In general, these pathogens are considered susceptible to tetracyclines, fluoroquinolones (FQs), and macrolides. Acquired resistance against several of these classes has been described, but studies on the antimicrobial susceptibility profiles and resistance mechanisms of genital mycoplasmas are still scarce and cover only some geographic regions.

To our knowledge, data on the antimicrobial susceptibility of genital mycoplasmas isolated in Switzerland are completely lacking. More importantly, information concerning the spread of spe-
cific clones at the international level is urgently needed (16). Therefore, the aim of this study was to fill these gaps by analyzing the Ureaplasma isolates detected among Swiss people.

MATERIALS AND METHODS

Clinical specimens. Clinical samples were collected between February and April 2014, in two microbiology laboratories located in Bern, Switzerland (i.e., the Institute for Infectious Diseases, University of Bern, Bern, and laboratoriums in the Bern University Hospital). Specimens were obtained from the urogenital tracts of patients (26 men and 114 women) who visited the Bern University Hospital (n = 7) or several outpatient practices (n = 133).

Species identification and antimicrobial susceptibility tests. Clinical samples were routinely processed using the Mycoplasma IST 2 kit (bio-Mérieux) for identification (ID) and antimicrobial susceptibility tests. Samples were processed using the Mycoplasma IST 2 kit (bio-Mérieux) for identification (ID) and antimicrobial susceptibility tests (ASTs) for U. urealyticum/U. parvum and/or M. hominis (17). AST results were interpreted according to the criteria set by the IST 2 kit (see the legend to Fig. 1 for interpretative criteria). U. urealyticum/U. parvum strains that were not susceptible to FQs and/or macrolides (n = 15), along with 10 pan-susceptible isolates, were stored at −80°C for further characterization. Since the IST 2 kit cannot distinguish between U. urealyticum and U. parvum species, the ID of these 25 strains was obtained by sequencing the 16S rRNA genes (18). Genomic extraction was performed using a QIAamp DNA minikit (Qiagen). For the aforementioned 15 nonsusceptible isolates, MICs for ciprofloxacin (CIP) and azithromycin (AZI) were determined with the broth microdilution method, following Clinical and Laboratory Standards Institute (CLSI) guidelines (19).

Analysis of quinolone and macrolide resistance mechanisms. For all FQ-nonsusceptible U. urealyticum and U. parvum isolates (n = 15) (Table 1), the quinolone resistance-determining regions (QRDRs) of gyrA, gyrB, parC, and parE genes were studied by PCR/DNA sequencing, as described previously (20). The parE gene was also analyzed with primers designed in this study (parEnew2-F, 5’-GCAATTGGTTGCACGAG ATGCT-3’; parEnew2-R, 5’-TGCCATTTCTAAATGAGCCGA-3’). All macrolide-nonsusceptible U. urealyticum and U. parvum isolates (n = 4) (Table 1) underwent PCR amplification and sequencing of both 23S rRNA alleles, as well as the genes encoding ribosomal proteins L4 and L22 (21). Two U. parvum isolates susceptible to both FQs and macrolides (ID59 and ID70 in Table 1) were used as controls.

Sequences were analyzed using DNAStar Lasergene software and were translated into protein sequences (http://ch.expasy.org). Amino acid substitutions in GyrA, GyrB, ParC, ParE, L4, and L22, as well as nucleotide mutations in the 23S rRNA alleles, were identified by comparison with wild-type sequences (GenBank accession number CP001184 for U. urealyticum and accession number AF222894 for U. parvum). Analysis of clonality. For the 25 U. urealyticum/U. parvum strains stored at −80°C, a PCR-based method was used for subtyping (U. urealyticum) and definition (U. parvum) of the serovars (6). A multilocus sequence typing (MLST) scheme (involving fshH, rpl22, vasB, and thrS genes) was also implemented for the same isolates (16).

Phylogenetic analysis of the detected sequence types (STs) was performed using MEGA 5.0 software. Briefly, the concatenated partial sequence of the four housekeeping genes (1,852 bp in total; 1,861 bp if the insertions were considered) from U. urealyticum and U. parvum isolates with different STs were used to construct a phylogenetic tree based on the number of nucleotide differences, implementing the neighbor-joining method with bootstrap tests (1,000 replicates).

Nucleotide sequence accession numbers. Five new alleles have been deposited in GenBank (accession numbers KR063735 and KR063736 for two fshH alleles and accession numbers KR063732 to KR063734 for three rpl22 alleles).

RESULTS AND DISCUSSION

In the past decade, U. urealyticum, U. parvum, and M. hominis have received increased attention because of their associations with urogenital infections, adverse pregnancy outcomes, preterm birth, and postpartum infections (1–3). Due to the frequent implementation of molecular tests that only identify the causative pathogens (22), these clinical conditions are usually treated with empirical therapy based on the use of macrolides, tetracyclines, or FQs (23, 24). However, data regarding the antibiotic susceptibility patterns of genital mycoplasmas are scarce, and local statistics particularly are needed to establish effective treatments. Therefore, one goal of the present study was to analyze for the first time the antimicrobial susceptibility profiles of contemporary genital mycoplasma isolates collected in Switzerland.

Of 140 samples, 103 (74%) were confirmed to be positive for U. urealyticum/U. parvum, whereas 21 (15%) were positive for both U. urealyticum/U. parvum and M. hominis. Since no pure cultures of M. hominis were obtained (and their numbers were small), only AST results for U. urealyticum/U. parvum were considered. As shown in Fig. 1, the following rates of nonsusceptibility for U. urealyticum/U. parvum were recorded using the IST 2 kit: CIP, 19.4%; ofloxacin (OFL), 9.7%; clarithromycin (CLA), 4.9%; erythromycin (ERY), 1.9%; AZI, 1%. None of the isolates showed reduced susceptibility to the more recently developed macrolides ( josamycin [JOS] and pristinamycin [PRI]) or the tetracyclines ( tetracycline [TET] and doxycycline [DOX]). These overall figures indicate that the standard treatments for urogenital infections due to Ureaplasma spp., as suggested by the Swiss recommendations (i.e., AZI or DOX), should lead to effective clinical outcomes in most cases (24).

We also positively note that the overall Swiss resistance rates seem to be low, compared to those for other countries. For instance, a recent Italian study investigating U. urealyticum strains isolated from female genital samples indicated the following resistance rates: CIP, 41%; ERY, 19%; CLA, 15%; OFL, AZI, TET, DOX, JOS, and PRI overall, <10% (12). Another Italian study, from De Francesco et al., obtained consistent results (10). Two Chinese analyses reported FOQ resistance rates of >40% for Ureaplasma spp., while rates of resistance to macrolides and tetracyclines were <30% and <10%, respectively (8, 9). In South Africa, Ureaplasma isolates had the following resistance rates: levofloxa
cin, 41%; moxifloxacin, 2%; ERY, 80%; TET, 73% (11). In Croatia, U. urealyticum strains showed nonsusceptibility rates of 22%, 8%, and 3% for OFL, AZI, and DOX, respectively (14). However, we emphasize that possible inconsistencies in resistance rates among the aforementioned studies could occur due to the use of different methodologies (i.e., Mycoplasma IST 2 kit [10, 12, 13] versus broth microdilution [25]) and/or different criteria for interpretation for the susceptibility results (i.e., those used for the Mycoplasma IST 2 kit [10, 12, 13] versus those of the CLSI [9, 11, 19]). As shown in this work (Table 1), conflicting results from the IST 2 kit and standard broth microdilution were observed for CIP and AZI (i.e., most of the isolates routinely reported as nonsusceptible to these antibiotics were actually fully sensitive). Therefore, rates of nonsusceptibility to FQs and macrolides might be underestimated using the IST 2 kit. Larger comparative studies should address these clinically important discrepancies.

Overall, in most countries the highest resistance rates have been recorded against FQs (8–14). This is undoubtedly due to their empirical overuse in the community (e.g., for urinary and respiratory tract infections), which contributes to the selection of amino acid substitutions in the QRDRs of DNA gyrase (GyrA and GyrB) and DNA topoisomerase IV (ParC and ParE) (20, 26, 27).
TABLE 1 Clonal distribution, subtypes, antibiotic phenotypes, and molecular characterization of 25 *Ureaplasma* isolates (including those not susceptible to FQs and/or macrolides; *n* = 15) collected in Bern, Switzerland, in 2014.

<table>
<thead>
<tr>
<th>Strain no.</th>
<th>Sample type(s)</th>
<th>Sex/age (yr)</th>
<th>Species(s)</th>
<th>MLST result</th>
<th>Antimicrobial susceptibility with IST 2 kit&lt;sup&gt;a&lt;/sup&gt;</th>
<th>QRDR analysis result&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Macroline resistance trait</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ST</td>
<td>CIP OFL CLA ERY AZI JOS PRI TET DOX</td>
<td>CIP AZI GyrA GyrB ParC ParE</td>
<td>25S rRNA L4 L22</td>
</tr>
<tr>
<td>6</td>
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<td>F/22</td>
<td>UUA</td>
<td>100&lt;sup&gt;c&lt;/sup&gt; 40&lt;sup&gt;c&lt;/sup&gt; 11&lt;sup&gt;c&lt;/sup&gt; 4 4</td>
<td>Sty-1</td>
<td>R I I I S S S S</td>
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<tr>
<td>41</td>
<td>SEM</td>
<td>M/35</td>
<td>UUA</td>
<td>Un 4 3 4 NA 11</td>
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<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
</tr>
<tr>
<td>55</td>
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<td>F/34</td>
<td>UUA</td>
<td>101&lt;sup&gt;c&lt;/sup&gt; 41&lt;sup&gt;c&lt;/sup&gt; 3 4 11</td>
<td>Sty-1</td>
<td>I S S S S S S S</td>
<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
</tr>
<tr>
<td>58</td>
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<td>F/34</td>
<td>UUA</td>
<td>54 6 3 4 11</td>
<td>Un I I S S S S S S</td>
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<td>Both WT WT WT</td>
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<td>Sty-1</td>
<td>I I S S S S S S</td>
<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
</tr>
<tr>
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<td>UUA</td>
<td>47 5 3 4 4</td>
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<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
</tr>
<tr>
<td>76</td>
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<td>UUA</td>
<td>9 4 3 4 4</td>
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<td>UUA</td>
<td>101&lt;sup&gt;c&lt;/sup&gt; 41&lt;sup&gt;c&lt;/sup&gt; 3 4 11</td>
<td>Sty-1</td>
<td>R I R I I S S S S</td>
<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
</tr>
<tr>
<td>109</td>
<td>VAG</td>
<td>F/17</td>
<td>UUA</td>
<td>102&lt;sup&gt;c&lt;/sup&gt; 6 2 2 11</td>
<td>Sty-1</td>
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<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
</tr>
<tr>
<td>11</td>
<td>CER</td>
<td>F/26</td>
<td>UPA</td>
<td>2 2 1 1 1</td>
<td>SV-1</td>
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<td>≤0.25 (S) ≤0.064 (S) WT WT WT Val417Thr</td>
</tr>
<tr>
<td>52</td>
<td>M/34</td>
<td>UPA</td>
<td>1 1 1 1 1</td>
<td>SV-3/14</td>
<td>I S S S S S S</td>
<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
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</tr>
<tr>
<td>53</td>
<td>SEM</td>
<td>M/19</td>
<td>UPA</td>
<td>38 2 1 1 1</td>
<td>SV-3/14</td>
<td>S S S S S S S S</td>
<td>— — — — — — —</td>
</tr>
<tr>
<td>59</td>
<td>CER/VAG</td>
<td>F/36</td>
<td>UPA</td>
<td>103&lt;sup&gt;c&lt;/sup&gt; 1 12&lt;sup&gt;c&lt;/sup&gt; 1 1</td>
<td>SV-6</td>
<td>S S S S S S S S</td>
<td>— — — — — — —</td>
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<tr>
<td>67</td>
<td>VAG</td>
<td>F/36</td>
<td>UPA</td>
<td>4 2 2 1 1</td>
<td>SV-1</td>
<td>I S S S S S S S</td>
<td>— — — — — — —</td>
</tr>
<tr>
<td>70</td>
<td>CER/VAG</td>
<td>F/32</td>
<td>UPA</td>
<td>104&lt;sup&gt;c&lt;/sup&gt; 1 1 1 2</td>
<td>SV-3/14</td>
<td>S S S S S S S S</td>
<td>— — — — — — —</td>
</tr>
<tr>
<td>71</td>
<td>CER</td>
<td>F/26</td>
<td>UPA</td>
<td>59 9 1 1 1</td>
<td>SV-1</td>
<td>S S S S S S S S</td>
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<td>78</td>
<td>SEM</td>
<td>M/29</td>
<td>UPA</td>
<td>104&lt;sup&gt;c&lt;/sup&gt; 1 1 1 2</td>
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<td>— — — — — — —</td>
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<td>1 (S) ≤0.064 (S) WT WT WT WT</td>
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<tr>
<td>114</td>
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<td>M/37</td>
<td>UPA</td>
<td>105&lt;sup&gt;c&lt;/sup&gt; 2 1 1 2</td>
<td>SV-1</td>
<td>S S S S S S S S</td>
<td>2 (I) 0.5 (I) WT WT WT WT Val417Thr</td>
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<td>F/40</td>
<td>UPA</td>
<td>106&lt;sup&gt;c&lt;/sup&gt; 2 13&lt;sup&gt;c&lt;/sup&gt; 1 1</td>
<td>SV-6</td>
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<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
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<td>134</td>
<td>CER</td>
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<td>UPA</td>
<td>107&lt;sup&gt;c&lt;/sup&gt; 2 1 9 1</td>
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<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
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<tr>
<td>153</td>
<td>CER</td>
<td>F/33</td>
<td>UPA</td>
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<td>≤0.25 (S) ≤0.064 (S) WT WT WT WT</td>
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<td>F/41</td>
<td>UPA</td>
<td>4 2 2 1 1</td>
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<td>S S S S S S S S</td>
<td>— — — — — — —</td>
</tr>
<tr>
<td>141</td>
<td>SEM</td>
<td>M/33</td>
<td>UPA</td>
<td>22 1 2 1 1</td>
<td>SV-6</td>
<td>R I S S S S S S</td>
<td>4 (R) ≤0.064 (S) WT WT Ser83Leu WT</td>
</tr>
</tbody>
</table>

<sup>a</sup>GEN, genital specimen not better defined; VAG, vaginal swab; CER, cervical swab, SEM, semen.

<sup>b</sup>M, male; F, female.

<sup>c</sup>Species identification was performed by sequencing the 16S rRNA genes. UUA, *U. urealyticum*; U. parvum.

<sup>d</sup>ST, sequence type; Un, undetermined; NA, not amplified.

<sup>e</sup>Sy, subtype; SV, serovar.

<sup>f</sup>AST results obtained with the Mycoplasma IST 2 kit (bioMérieux) and interpreted according to the manufacturer’s criteria (see the legend to Fig. 1 for breakpoints). CIP, ciprofloxacin; OFL, ofloxacin; CLA, clarithromycin; ERY, erythromycin; AZI, azithromycin; JOS, josamycin; PRI, pristinamycin; TET, tetracycline; DOX, doxycycline; R, resistant; I, intermediate; S, susceptible.

<sup>g</sup>MICs obtained in broth microdilution assays according to CLSI guidelines (tests repeated two times). Since interpretative criteria for CIP and AZI are not available from CLSI (19), MICs were interpreted according to the IST 2 kit criteria (see the legend to Fig. 1).

<sup>h</sup>New STs; numbering starts from the last ST reported by Zhang et al. (16) (i.e., ST99).

<sup>i</sup>New alleles; numbering starts from the last allele (i.e., 39) and the last *rpl22* allele (i.e., 10) reported by Zhang et al. (16). The five new alleles have been deposited in GenBank under accession numbers KR063732 to KR063734 for *ftsH* alleles and KR063735 and KR063736 for *rpl22* alleles.

<sup>j</sup>These isolates were used as negative controls for all PCR/DNA sequencing tests for QRDR and macrolide resistance genes.

<sup>k</sup>—, not performed.
In our *U. parvum* strains, we found the substitutions Ser83Leu in ParC and Val417Thr in ParE, whereas the previously unreported Thr417Val in ParE was detected in *U. urealyticum* (Table 1) (27). However, we noted with surprise that only 5 of 15 CIP-nonsusceptible isolates (MICs of ≥2 µg/ml by using the IST 2 kit) had amino acid substitutions in the QRDRs. This phenomenon was observed previously and was ascribed to mechanisms not yet recognized (e.g., altered membrane permeability); however, we emphasize that the IST 2 kit might overrate the FQ resistance (i.e., high MICs that are actually in the susceptible range with the microdilution method). With regard to the QRDR substitutions found in the five isolates, only the well-described Ser83Leu substitution in ParC (*U. parvum* ID141 [ST22 and serovar 6]) conferred resistance to CIP (MIC of 4 µg/ml with the microdilution method) (25, 28), whereas both Thr417Val (for *U. urealyticum*) and Val417Thr (for *U. parvum*) ParE substitutions had predicted small effects on the MICs (Table 1) (27).

Mutations in the two copies of 23S rRNA or, more frequently, amino acid substitutions in the L4 and L22 ribosomal proteins were linked previously to macrolide resistance. However, studies focusing on these molecular aspects are scarce (15, 21, 29–31). In the present work, we analyzed the aforementioned resistance traits for four *Ureaplasma* isolates showing nonsusceptibility to macrolides (MICs of ≥2 µg/ml for CLA or ERY with the IST 2 kit); none of the isolates possessed substitutions in L4 or L22 or mutations in the 23S rRNA copies (Table 1). These unexpected findings may be explained by the fact that (i) our four isolates were actually susceptible to macrolides, according to the CLSI criteria (MICs of 0.064 µg/ml for ERY) (19), and (ii) all macrolide-nonsusceptible strains were truly sensitive when tested with the microdilution method, with most of the AZI MICs being ≤0.064 µg/ml (Table 1). In contrast, *Ureaplasma* isolates with one of the aforementioned chromosomal mechanisms of resistance are usually highly resistant (e.g., MICs of ≥128 µg/ml for ERY) (15).

For 25 of 103 isolates (i.e., 9 *U. urealyticum* isolates and 16 *U. parvum* isolates), we also obtained the serovars and explored the distribution of STs by analyzing the isolates with a MLST method recently developed by Zhang et al. (16). This overall information is essential for establishing whether certain *Ureaplasma* lineages are spreading clonally and, more importantly, whether they are associated with specific and/or more severe clinical conditions. Based on their MLST scheme, Zhang et al. (16) indicated that *Ureaplasma* strains from China are split into two clonal complexes, which are highly congruent with the taxonomic differences between *U. parvum* and *U. urealyticum* species. Notably, *U. parvum* and its two major clones (ST1 and ST22) are found more often in asymptomatic infections than *U. urealyticum* (e.g., ST9 and ST47). However, we note that information regarding the distribution of STs for *Ureaplasma* spp. is limited to the Chinese data provided by the aforementioned authors (14 reference strains and 269 isolates analyzed), and nothing is known about other geographical regions (16, 32).

As shown in Table 1, our results indicate that, although numerous new STs in both *U. urealyticum* (from ST100 to ST102) and *U. parvum* (from ST103 to ST107) were identified, the main *Ureaplasma* clones recently observed in China are also present among Swiss people. In particular, ST4 (including serovars 1, 6, and 3/14) was the most prevalent among *U. parvum* isolates, but ST1 (serovar 3/14), ST2 (serovar 1), ST22 (serovar 6), ST38 (serovar 3/14), and ST58 (serovar 1) were also detected. With regard to *U. urealyticum*, unique ST9 (subtype 2), ST47 (subtype 1), and ST34 (not typeable with the PCR methodology implemented) isolates were
found. Therefore, according to the MLST findings, the two patient populations (Chinese and Swiss) share several clones of \textit{U. parvum} and \textit{U. urealyticum}. This finding raises the question of whether specific hyperendemic lineages of \textit{Ureaplasma} spp. can spread worldwide (e.g., via sexual intercourse) and then adapt themselves well to the urogenital tracts of different populations. In support of this speculation, the phylogenetic analysis performed using MEGA 5.0 with 6 \textit{U. urealyticum} and 11 \textit{U. parvum} isolates with different STs indicated that most of the novel STs found in the present study are strongly related to the ancestors (ST1 for \textit{Ureaplasma urealyticum} and ST4 for \textit{Ureaplasma parvum}) and to the very prevalent Chinese variants (e.g., ST4, ST9, and ST22) (Fig. 2).

In conclusion, this study fills up the lack of Swiss data regarding the antibiotic susceptibility of \textit{Ureaplasma} spp. responsible for urogenital infections, indicating a lower prevalence of resistant isolates, compared to other countries. We surprisingly detected numerous STs already observed in China, but these intriguing results could not be matched with those from other geographic regions due to the complete absence of studies focusing on this matter. Unfortunately, our study does not provide adequate clinical data to establish the extent of infection or colonization and the potential link with specific STs of \textit{U. urealyticum} and \textit{U. parvum} among our patients. Large combined microbiological and clinical studies should address these important aspects in the near future.

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**REFERENCES**


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