Prevalence and Impact of *Ureaplasma Urealyticum* on Infertility

Nedjoua Sekhri-Arafa[1*], Rihab Traïkia[2], Douaa Zaarour[2]

Abstract

Background: Infertility is a significant global health issue, with sexually transmitted infections (STIs) identified as potential contributing factors. *Ureaplasma urealyticum*, a common urogenital bacterium, is implicated in various reproductive complications. This study investigates the prevalence and impact of U. urealyticum in infertility cases in Constantine, Algeria, focusing on both male and female patients. Methods: A combined prospective and retrospective analysis was conducted from 2020 to 2023, encompassing 480 samples from patients at a private medical laboratory. Samples were collected through endocervical and urethral swabs, as well as semen collection. The MYCOFAST RevolutioN ATB+ kit was utilized for the detection and analysis of U. urealyticum and Mycoplasma hominis. Results: U. urealyticum was found to be the predominant pathogen, responsible for 99.41% of infections, while M. hominis accounted for only 0.59%. The infection rate was higher in men compared to women, with a male/female ratio of 1.2. The most affected age group was 34-44 years. Despite the overall lower prevalence of positive cases (35.62%), the study highlights the necessity for continued vigilance and preventive measures against STIs. Conclusion: The study identifies U. urealyticum as the primary species responsible for urogenital infections in both men and women in the studied population. The findings underscore the importance of STI monitoring and preventive strategies, even in regions with relatively lower prevalence rates. The use of the MYCOFAST RevolutioN ATB+ kit proved effective in the rapid detection of these pathogens, facilitating further etiological and epidemiological research. Ongoing research is essential to enhance understanding and develop interventions to mitigate the impact of Ureaplasma infections on reproductive health.

Keywords: Infertility, Sexually transmitted infections, Mycoplasmas, *Ureaplasma urealyticum*

Significance | Infertility is a global concern linked to STIs like *Ureaplasma urealyticum*, necessitating ongoing research to improve reproductive health outcomes.

*Correspondence. SEKHRI-ARAFA Nedjoua , Immunology and Biologica Activities Of Natural Substances, Department of Microbiology, Faculty of Natural and Life Sciences, University Mentouri Brothers Constantine, Algeria
E-mail:
arafa.nedjoua@umc.edu.dz,sekhriarafa@hotmail.cor

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1.Introduction

Infertility, defined as the inability to conceive after 12 months of regular unprotected intercourse, represents a significant global health concern. The World Health Organization (WHO) estimates that around 17.5% of adults worldwide encounter infertility issues, emphasizing the widespread nature of this condition (WHO, 2023). This prevalence is consistent across both high-income and low-income countries, affecting approximately one in six individuals during their reproductive years (WHO, 2023). Among the myriad factors contributing to infertility, sexually transmitted infections (STIs) emerge as a major cause. Often asymptomatic, STIs can lead to severe reproductive complications if left untreated (Anwar & Anwar, 2016; Kissinger, 2015). One STI of particular interest is *Ureaplasma urealyticum*, a microorganism typically considered a commensal organism in healthy individuals. Despite its usually

Author Affiliation.
[1] Immunology and Biological Activities Of Natural Substances, Department of Microbiology, Faculty of Natural and Life Sciences, University Mentouri Brothers Constantine, Algeria.
[2] Department of Microbiology, Faculty of Natural and Life Sciences, University Mentouri Brothers Constantine, Algeria.

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harmless presence, *Ureaplasma urealyticum* has been linked to several reproductive disorders, including non-gonococcal urethritis, bacterial vaginosis, and prostatitis (Taylor-Robinson, 1996). More critically, Ureaplasma infections have been associated with adverse pregnancy outcomes such as chorioamnionitis, premature delivery, spontaneous abortion, and stillbirth (Bharat et al., 2015). The often asymptomatic nature of these infections allows them to persist unnoticed and be transmitted between partners unknowingly, posing a significant risk, particularly for women who are more likely to seek medical care for gynecological issues (Song et al., 2014).

Understanding the prevalence and impact of *Ureaplasma urealyticum* on reproductive health is crucial for developing effective clinical practices and public health strategies. This study aims to address this knowledge gap by prospectively and retrospectively analyzing data from 2020 to 2023 to assess the prevalence of *Ureaplasma urealyticum* in infertility cases. The focus is specifically on a private laboratory in Constantine, providing a unique opportunity to explore the local epidemiology of this infection and its role in infertility (Szamatowicz & Szamatowicz, 2020).

By thoroughly examining the prevalence and implications of *Ureaplasma urealyticum* on infertility, this research seeks to enhance our understanding of its role in reproductive health. The findings from this study could significantly inform clinical practices and public health policies aimed at improving the diagnosis, treatment, and prevention of Ureaplasma-related infertility. Ultimately, the goal is to contribute to better reproductive outcomes for individuals affected by this infection, providing them with the necessary medical interventions to address and manage their infertility issues effectively.

Infertility continues to affect a substantial portion of the global population, particularly influenced by STIs like *Ureaplasma urealyticum*, it becomes increasingly important to conduct focused research on its prevalence and impact. This study's findings will not only provide valuable insights into the epidemiology of *Ureaplasma urealyticum* but also pave the way for more targeted and effective healthcare interventions, thereby improving reproductive health outcomes worldwide.

2. Material and methods

2.1 Study design

The collection of samples for this study was performed by either a gynecologist or a midwife, following specific protocols for endocervical sampling in women, male urethral sampling, semen collection, and first urine stream collection.

2.2 Endocervical Sampling in Women

Endocervical sampling in women involves several steps to ensure the accuracy and integrity of the sample. Initially, excess mucus is removed from the cervical os using a cleaning swab, which is discarded after use. The specimen collection swab is then introduced into the endocervical canal and rotated gently for 10 seconds to ensure adequate sampling. Care is taken to remove the swab without contacting the vaginal mucosa to avoid contamination. The swab is then placed in a vial containing Ureaplasma Mycoplasma Transport (UMMt) medium, and the swab rod is carefully broken at the cut line to prevent contents from flying out. The UMMt medium is stored at room temperature (18-25°C) for up to 20 hours or at 2-8°C for up to 56 hours.

2.3 Male Urethral Sampling

For male urethral sampling, the meatus is first cleaned to prepare for the sample collection. A fine swab is introduced into the urethral meatus, inserted 2 to 4 cm deep, and rotated slightly to ensure adequate sampling. The swab is then placed in a vial containing UMMt medium, and the swab is broken at the cut line. The UMMt medium is stored at room temperature (18-25°C) for up to 20 hours or at 2-8°C for up to 56 hours.

2.4 Semen Collection

Semen collection takes place in the laboratory, where the patient collects his semen through masturbation into a hermetically sealed bottle. The collected semen is then incubated at a temperature of 37°C for 15 minutes to maintain the viability of the sample.

2.5 First Urine Stream Collection

The first urine stream collection requires the patient to refrain from urinating for at least two hours prior to collection. The first stream of urine is collected in a sterile bottle without any preservatives. The sample must be sent to the laboratory within an hour, maintained at room temperature to preserve its integrity.

3. Diagnosis of Ureaplasma urealyticum

The diagnosis of *Ureaplasma urealyticum* is performed using the MYCOFAST RevolutioN ATB+ method, which is based on the ability of *Ureaplasma urealyticum* and Mycoplasma hominis to metabolize urea and arginine, respectively. This method involves observing a color change in the liquid medium, indicated by phenol red, from yellow-orange to red, reflecting the alkalization of the medium due to ammonia release.

4.Procedure

The procedure begins with bringing the reagents to room temperature for 20 to 30 minutes. Following this, 100 µl of seeded UMMt medium is distributed into wells 1-24, along with 2 drops of mineral oil in each well. The gallery is then covered by engaging the lid to ensure a closed system. Any excess UMMt vial is stored at 2-8°C for at least 48 hours for possible verification. The gallery is incubated at 37°C for 24 hours, with the incubation period extended up to 48 hours only if the liquid samples remain negative at 24 hours. Finally, the results for U. urealyticum and M. hominis counts are read at 24 hours to determine the presence and concentration of the organisms.

3. Results

3.1 Interpretation of MYCOFAST RevolutioN ATB+ Kit Results

The MYCOFAST RevolutioN ATB+ kit is utilized for detecting urogenital mycoplasmas based on observed color changes in the growth medium. A red color indicates alkalinization due to mycoplasma presence, while a persistent yellow color signifies absence of growth. For samples initially negative at 24 hours but positive upon re-evaluation at 48 hours, only the presence, not quantity, of mycoplasmas is reported.

3.2 Counting (Wells 1, 2, and 3)

The interpretation of color changes in the wells is based on specific criteria: Well 1 indicates U. urealyticum at 10^3 UCC/ml, while Wells 1 and 2 indicate U. urealyticum at ≥10^4 UCC/ml. Well 3 indicates M. hominis at ≥10^4 UCC/ml. Pathological thresholds for mycoplasmas are established as follows: U. urealyticum levels ≥10^4 UCC/ml in urethral samples and ≥10^3 UCC/ml in the initial urine or semen stream are considered abnormal. Similarly, M. hominis levels ≥10^4 UCC/ml in cervico-vaginal samples are deemed abnormal according to defined guidelines**.**

3.3 Antibiotic Sensitivity Tests (Wells 4 to 24)

The antibiotic sensitivity of mycoplasmas is determined by observing growth in wells containing various antibiotics. A yellow medium indicates growth inhibition, suggesting susceptibility, while a red medium indicates resistance. Antibiotic susceptibility and resistance are evaluated according to criteria established by the Clinical and Laboratory Standards Institute (CLSI). The results (Figure 1) indicate that the U. urealyticum strain is susceptible to Telithromycin, Tetracycline, Azithromycin, Pristinamycin, and Josamycin, but resistant to Clindamycin, Levofloxacin, Moxifloxacin, and Ofloxacin.

3.4 Distribution of Samples According to Results

Out of 480 samples received, 171 (35.62%) tested positive for mycoplasmas, while 309 (64.38%) were negative (Figure 2).

3.4.1 Breakdown of Samples by Type

Among the 480 samples, 218 were endocervical samples from women, and 262 were semen samples from men (Figure 3).

3.4..2 Distribution of Samples by Gender

Of the 480 patients, 218 (45.42%) were female, and 262 (54.58%) were male (Figure 4).

3.4.3 Distribution of Results by Presence of Mycoplasmas

Out of the 171 positive samples, 170 (99.41%) were *Ureaplasma urealyticum*, and only 1 (0.59%) was Mycoplasma hominis (Figure 5).

3.4.4 Distribution of Positive Results by Mycoplasma Species

The majority of positive results were attributed to U. urealyticum (Figure 6).

3.4.5 Distribution of Positive Ureaplasma urealyticum Results by Age

Positive results for U. urealyticum were observed across various age groups, with women averaging 34 years (range: 24-44) and men averaging 40 years (range: 24-55). In women, the age distribution was 30 cases (40.54%) aged 24-34, 43 cases (58.11%) aged 34-44, and one case aged 46. In men, 28 cases (29.16%) were aged 24-34, 41 cases (42.71%) aged 34-44, and 27 cases (28.13%) aged 44 and older (Figure 7).

3.4.6 Distribution of Positive Ureaplasma urealyticum Results by Gender

Among the 170 positive U. urealyticum results, 75 (44%) were female and 96 (56%) were male, indicating a male-to-female ratio of 1.2 (Figure 8), suggesting a higher infection rate among men.

4. Discussion:

Ureaplasma urealyticum is a bacterium commonly found in the urogenital tract and nasopharynx of humans. This species can have significant implications depending on its concentration within the genitourinary system, leading to various conditions such as urethritis and prostatitis in men, and cervicitis and salpingitis in women (Bharat et al., 2015; Gimenes et al., 2014). Understanding its prevalence, transmission dynamics, and impact on reproductive health is crucial for effective clinical management and public health strategies.

The prevalence of U. urealyticum varies widely across populations and geographical regions. Our study observed a 35.62% positive rate for mycoplasmas among 480 samples, indicating a notable presence of these pathogens in our study cohort (Figure 2). This finding is consistent with previous research highlighting the ubiquitous nature of U. urealyticum in genital tract infections (Van Den Brule et al., 2006; Gupta et al., 2009).

In clinical settings, higher concentrations of U. urealyticum can disrupt the delicate balance of vaginal flora, potentially leading to symptomatic infections when present in significant quantities. This is particularly pertinent in cases of infertility, where U. urealyticum has been implicated as a factor contributing to reproductive health issues in both men and women (Gupta et al., 2009).

U. urealyticum is primarily transmitted through sexual intercourse, underscoring its classification as a sexually transmitted infection (STI) (Gimenes et al., 2014). The bacterium's ability to colonize and proliferate in the urogenital tract depends on various factors, including the individual's immune status and the presence of other concurrent infections.

Our study noted higher infection rates in males compared to females (Figure 8), a trend that contrasts with some earlier findings. This discrepancy may stem from differences in sexual behavior, biological susceptibility, or regional variations in healthcare practices (Zheng et al., 2020; He et al., 2016).

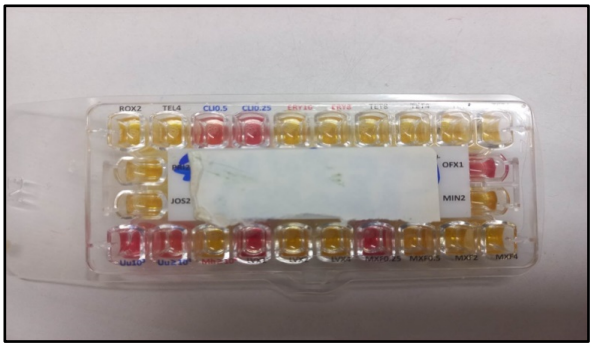

Figure 1 . Positive result of the MYCOFAST RévolutioN ATB+ test.

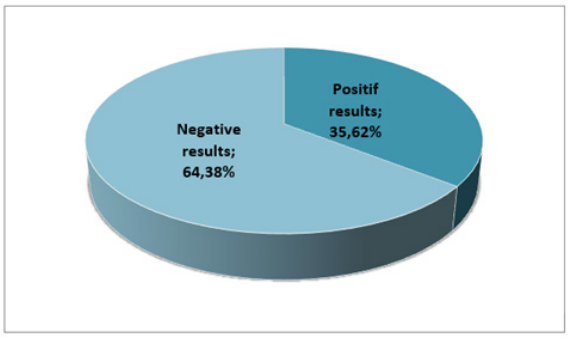

Figure 2. Distribution of samples according to the results obtained (+/-) (n=480)

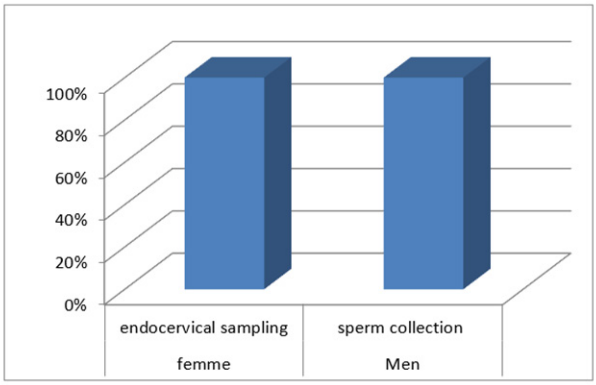

Figure 3 . Breakdown of direct debits by type of direct debit (n=480).

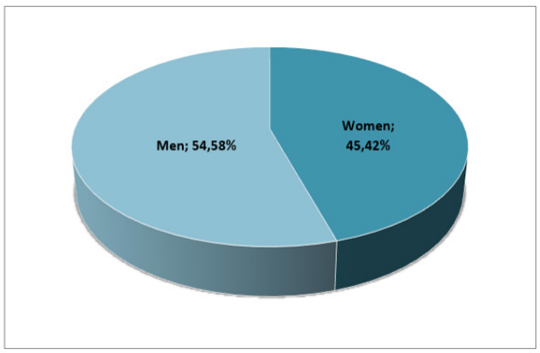

Figure 4: Distribution of samples by gender (n=480).

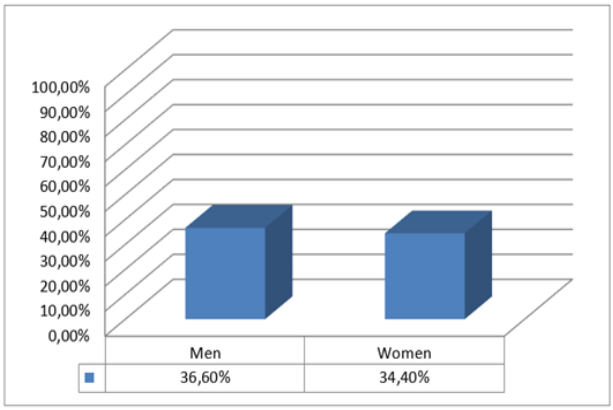

Figure 5. Distribution of results according to the presence of mycoplasmas (n=171)

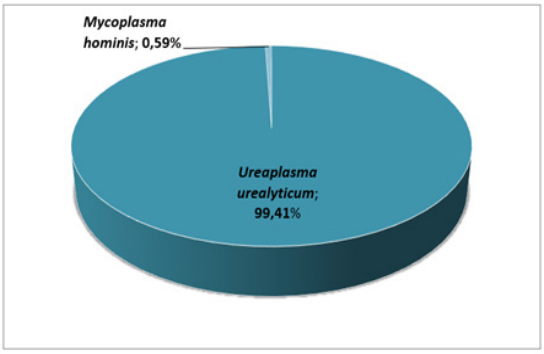

Figure 6 . Distribution of positive results according to the species of mycoplasma incriminated (n=171).

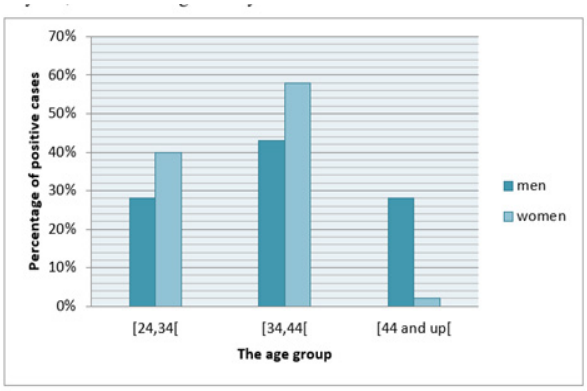

Figure 7. Distribution of positive *Ureaplasmaurealyticum* results by age (n=171).

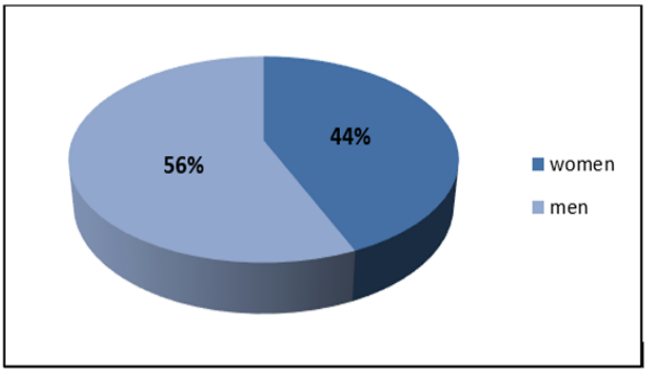

Figure 8. Distribution of positive *Ureaplasmaurealyticum* results by gender (n=171).

Accurate diagnosis of U. urealyticum infections is crucial for appropriate clinical management. In women, endocervical sampling is preferred for its ability to maximize the recovery of infected cells, thereby enhancing diagnostic sensitivity (Peeling & Embree, 2005; Sellors et al., 1991). Conversely, semen analysis in men not only detects the presence of infections but also provides insights into semen quality, crucial for fertility assessments and assisted reproductive technologies (Peeling & Embree, 2005; Andrade-Rocha, 2003).

The choice of sampling method influences the detection sensitivity and subsequent treatment strategies, highlighting the importance of standardized protocols in clinical microbiology.

The implications of U. urealyticum infections on reproductive health are multifaceted. In women, untreated infections can ascend through the reproductive tract, potentially leading to pelvic inflammatory disease (PID) and subsequent fertility complications (Van Den Brule et al., 2006). In men, the bacterium's presence in the genitourinary tract has been associated with prostatitis and impaired semen quality, impacting fertility outcomes (Andrade-Rocha, 2003).

Moreover, studies have shown a higher prevalence of U. urealyticum infections in women of childbearing age, suggesting a critical period for targeted screening and intervention strategies (Zheng et al., 2020). Understanding these age-related patterns aids in designing effective public health initiatives aimed at reducing the burden of urogenital infections in reproductive-aged individuals.

The global prevalence of U. urealyticum underscores its significance as a public health concern, necessitating comprehensive strategies for prevention, diagnosis, and treatment. Variations in prevalence rates across different populations highlight the need for tailored approaches in healthcare settings, considering regional epidemiological trends and socioeconomic factors influencing healthcare access and utilization.

Ureaplasma urealyticum remains a prevalent bacterium in the urogenital tract with significant implications for reproductive health. Advances in diagnostic techniques and understanding of transmission dynamics are essential for effective management and prevention of associated complications. Continued research efforts are crucial to elucidate the bacterium's pathogenesis and inform evidence-based practices in clinical and public health settings.

5. Conclusion

Infertility, a global health issue affecting approximately 17.5% of adults worldwide, is influenced by various factors, including sexually transmitted infections (STIs) like *Ureaplasma urealyticum*. This bacterium, typically considered commensal, has been implicated in conditions such as urethritis, prostatitis, cervicitis, and salpingitis, with severe implications for reproductive health, including pelvic inflammatory disease and adverse pregnancy outcomes. Our study highlighted a 35.62% prevalence of mycoplasmas among 480 samples, predominantly U. urealyticum, with higher infection rates in men than women. Accurate diagnosis through specific sampling methods is crucial for effective clinical management and underscores the need for targeted public health interventions to mitigate its impact on fertility outcomes worldwide.

Author contributions

N.S.A, R.T, & D.Z wrote, collected data, arranged data, and interpreted it; GM conceptualized the work; GM & HBS critically revised the manuscript; BJ, ST, GM, & HBS read and approved the final version of the manuscript.

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Competing financial interests

The authors have no conflict of interest.

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