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Trichomoniasis: A Neglected Sexually Transmitted Infection with Significant Risks to Reproductive Health

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ABSTRACT: Trichomoniasis, caused by *Trichomonas vaginalis*, remains one of the most prevalent yet neglected manuscrit worldwide. Despite its high global incidence, trichomoniasis is often underdiagnosed, underreported, and overlooked in public health initiatives. Emerging evidence accentuates its consequential significant risks to reproductive health, including adverse pregnancy outcomes, infertility, increased susceptibility to HIV and even cervical carcinoma. This short communication highlights the disease burden, clinical manifestations, diagnostic challenges, genetic polymorphism and long-term reproductive sequelae of trichomoniasis. Further, it emphasizes the urgent need for public awareness, improved screening facilities, interventions to target population to mitigate the reproductive health burden of this preventable yet neglected infection.

Keywords; Trichomoniasis, Neglected Sexually Transmitted Infection, Diagnostic Challenges, Reproductive Health Risks.

Article at a glance:
***Study Purpose**: To highlight the prevalence, risks, and diagnostic challenges of trichomoniasis.*
***Key findings:** Trichomoniasis is prevalent globally but often underdiagnosed, leading to significant reproductive health problems.*
***Newer findings:** Advances in molecular diagnostics improve detection, and genetic diversity in strains affects disease outcomes and treatment.*
***Abbreviations:** STIs: Sexually Transmitted Infections; SDI: Socio-Demographic Index; NGU: Nongonococcal Urethritis; HPV: Human Papilloma Virus; HSV: Herpes Simplex Virus; NAATs: Nucleic Acid Amplification Tests; CDC: Centers for Disease Control and Prevention; MTZ: Metronidazole; TIN: Tinidazole.*

INTRODUCTION

Trichomoniasis remains one of the most neglected but curable sexually transmitted infections (STIs) that are often overlooked. Its high prevalence and the frequency of coinfection with other STIs make trichomoniasis compelling global public health concern.[1] It is caused by *Trichomonas vaginalis* (*T. vaginalis*), a flagellated protozoan parasite that infects the human urogenital tract. Trichomoniasis is considered as the most prevalent nonviral sexually transmitted disease with global incidence of approximately 156 million each year, with higher rates in low-resource settings due to limited access to screening and treatment. It is common in some subpopulations and approximately one third of new infections occur in the WHO African region, followed by the region of the Americas.[2] From 1990 to 2021, the number of trichomoniasis cases increased by 73%, with the most significant rise observed in low socio-demographic index (SDI) regions.[3] Like other countries, trichomoniasis remains a neglected STI in Bangladesh too with varying prevalence across

different populations. In a recent study in Bangladesh, utilizing multiplex PCR testing from 2015 to 2022, found that 6.6% of STI-positive cases were due to *T. vaginalis*.[4] Several factors including asymptomatic cases, lack of awareness and access to treatment facilities and low sensitivity of conventional diagnostic tools, the actual prevalence is underestimated.[5] Despite its prevalence, especially among women of reproductive age ranging 15 to 49 years old, it receives comparatively less public health attention than other STIs like chlamydia, gonorrhea, or HIV. This neglect can have significant implications for individual as well as mass reproductive health.[6]

Pathology

The parasite colonizes within the squamous epithelium of the urogenital tract of men and women due to its unique biological adaptation capacity and destroys epithelial cells by direct cell contact and by the release of cytotoxic substances in addition to inflammation and alteration of vaginal microbiota. *T. vaginalis* has unique immune evasion mechanisms that include surface antigenic variation, production of proteolytic enzymes and biofilm formation. It requires vaginal pH of 5 - 5.5 for establishing infection (normal vaginal pH is 4 - 4.5) and young girls and menopausal women are not susceptible because their vaginal pH remains around 7. Affected individual mostly remains asymptomatic but more than 50% of women have vaginal discharge and about 10% of men have nongonococcal urethritis (NGU), prostatitis, and epididymitis. Symptomatic women usually complain of malodorous vaginal discharge, vulvovaginal soreness, itching and/or irritation and a 'strawberry cervix', characterized by punctate hemorrhagic lesions. In addition to reproductive tract symptoms, *T. vaginalis* infection has been increasingly associated with infertility and adverse pregnancy outcomes such as premature rupture of membranes, premature birth, low birth weight and also carries a risk of cervical cancer.[5, 6] Further, trichomoniasis has been recognized as a risk factor for increase transmission of other STIs including gonorrhea, human papillomavirus (HPV), herpes simplex virus (HSV) and most importantly the human immunodeficiency virus (HIV).[7]

Impact on Reproductive Health

Pregnancy complications (premature rupture of membranes, preterm delivery, and low birth weight baby)
Increased susceptibility to HIV
Pelvic inflammatory disease (PID)
Prostatitis and infertility
Increased risk of cervical carcinoma

Transmission

Sexually active people usually get trichomoniasis by having penile-vaginal sex with a partner suffering from trichomoniasis. Interestingly an asymptomatic infected partner can still carry and transmit the parasite. Newborn can acquire the infection from infected birth canal during vaginal delivery and may exhibit symptoms during the first 3 to 4 weeks of neonatal life.[8] The transmission and prevalence of trichomoniasis exhibit significant differences between males and females. Risk factors include having multiple sexual partners, engaging in unprotected sex, having a history of other STIs, use of intrauterine contraceptive devices and sharing sex toys without proper cleaning or protection. Other factors like smoking, poverty, low education, and being incarcerated have also been linked to higher prevalence.[9] The differences in incidence and prevalence of trichomoniasis among male and female may be due to both behavioral and physiological factors. Men tend to change partners more frequently and have earlier sexual initiation compared to women.[10] However, women are more severely affected by trichomoniasis because of their unique reproductive biology, which increases their risk of infertility, cervicitis, pelvic inflammatory disease and even cervical cancer following infection.[6] Although men are often asymptomatic, their ability to unknowingly transmit the infection highlights the need for more accessible and responsive testing for men.

Why does Trichomoniasis is Neglected?

Lack of awareness among public and healthcare providers
Underdiagnosis
Underreporting
Misconception of severity
Lack of routine screening
Not a reportable disease
Association with stigma
Gender bias in testing and research

Laboratory Diagnosis

Symptoms and signs of trichomoniasis are not adequately sensitive or specific for its diagnosis like other sexually transmitted diseases. Thus,

diagnostic laboratory testing is usually required to confirm the presence of the organism. Routine clinical diagnosis usually depends on microscopic observation of motile parasites in a wet mount vaginal fluid but unsatisfactory diagnostic sensitivity (44-68%) is a limiting factor. Prior to the advent of nucleic acid amplification tests (NAATs), culture in Diamond's medium was the gold standard with a sensitivity of 81–94% for diagnosis of *T. vaginalis*.[11] However, contamination with vaginal bacteria, viability dependence and long turnaround time are among the major limiting factors for culture. Culture systems, such as the InPouch® system (BioMed Diagnostics, White City, OR), have been developed to avoid contamination by placing the specimen in a two-chambered bag, allowing for simultaneous sampling for wet mount and culture.[12] To overcome disadvantages associated with conventional microscopy and culture techniques, NAAT has been introduced in the diagnosis of trichomoniasis which is highly sensitive and specific and also holds a promise to become the gold standard for laboratory detection. The Xpert® TV assay (Cepheid, Sunnyvale, CA) was the first *T. vaginalis* NAAT FDA approved for use in female urine, endocervical swab, and patient- and clinician-collected vaginal specimens as well as male urine. Diagnostic sensitivity and specificity for the Xpert® TV assay range from 99.5–100%.[13] Microfluidic Paper-based Analytical Devices (μPADs) detecting nucleic acids or antigens and CRISPR-based diagnostics (e.g., SHERLOCK, DETECTR) to detect *T. vaginalis* DNA with fluorescence or colorimetric readout are promising tools but currently under experimental stage and need further validation.[14, 15] Recently rapid diagnostic test (immunochromatographic assay) has been added as point-of-care test used usually in the STI clinics and in resource-limited situations but variable diagnostic sensitivity is a major limiting factor. Molecular diagnostic methods have tremendous positive impact not only in early and accurate diagnosis but also in its cost-effectiveness. Further, identification of genotype(s) of *T. vaginalis* through molecular tools and correlation of genotype with sociodemographic and clinical attributes of patients can add further value to understand the reasons underlying diversity in pathogenesis and treatment failure.[16]

Genetic Polymorphism

With approximately 60,000 protein-coding genes, *T. vaginalis* possesses a genome of 160 Mb with many repeated and transposable elements contained in the genome that can vary in position leading to genetic polymorphism and strain variations.[17] Recent advancements in the genetic analysis of *T. vaginalis* isolates revealed a strong link between the genetic polymorphism and the wide range of clinical outcomes in trichomoniasis, as well as its disease-related complications. Several methods of genotyping of the parasite revealed extensive genetic variation among *T. vaginalis* strains. Molecular studies consistently identified two predominant genotypes (Genotype I and Genotype II) of *T. vaginalis*. Evolutionarily, Genotype I is believed to be older than genotype II, as it displays greater genetic variation. Interestingly, both genotypes are found in similar proportions globally. Clinically, Genotype I tends to be associated with more pathogenic infections, while Genotype II has been linked to resistance to metronidazole, a common treatment for trichomoniasis. Certain genotypes have been linked to variations in disease severity and treatment response, suggesting that genetic diversity may influence clinical manifestations of trichomoniasis. Thus, the global prevalence and the health sequelae associated with *T. vaginalis* infections have necessitated the need to understand its genetic make-up. Recent advances in molecular typing methods through PCR and its related techniques like PCR-RFLP technique, based on the amplification of the actin gene, is considered a sensitive and reliable method for typing *T. vaginalis* isolates. With the advent of molecular techniques and tools scientists have a better understanding of its molecular epidemiology, genetic diversity, and population structure of *T. vaginalis*.[18, 19] Further, it has also provided a tool to study genetic relatedness between clinical samples, allows tracking of transmission routes, outbreaks and treatment failure versus reinfections.[20] Recent advances in genetic characterization of *T. vaginalis* isolates show that the extensive clinical variability in trichomoniasis and its disease sequelae are matched by significant genetic diversity in the organism itself, suggesting a connection between the genetic identity of isolates and their clinical manifestations.[21]

Management

The management of trichomoniasis continues to evolve, particularly in women. Centers for Disease Control and Prevention (CDC) treatment guidelines recommend a single 2-gram dose of oral metronidazole (MTZ) or tinidazole (TIN) as first-line

treatment for trichomoniasis in HIV-negative women and men. Oral MTZ 500 mg twice daily for 7 days is an alternative regimen. Emerging evidence suggests potential resistance to standard treatments in some cases, underscoring the need for monitoring. Persistent or recurrent infection due to antimicrobial-resistant *T. vaginalis* or other causes should be differentiated from reinfection from an untreated or insufficiently treated sexual partner.[6] A detailed patient history should be taken to assess the likelihood of reinfection. Following treatment failure, and if reinfection has been excluded, persistent or recurrent trichomoniasis has been treated successfully with longer courses or additional doses of the same medications used in standard therapy. Concurrent treatment is recommended for all sexual partners of patients with trichomoniasis, and it is critical for symptomatic relief, microbiologic cure, and prevention of transmission and reinfection.[22]

CONCLUSION

Even though it can cause serious reproductive issues, trichomoniasis is often viewed as a "mild" or "nuisance" infection that reduces the urgency for research, education, and screening programs. Findings highlight the growing burden of trichomoniasis and underscore the importance of integrating routine vaginal testing for trichomoniasis with gynecological examinations. Although trichomoniasis is a relatively common STI with many potential harmful effects, there is currently no regular screening for any population group except women living with HIV. Further, in recent years, many advances have been made in the epidemiology, diagnosis, and treatment of *T. vaginalis* and the focus of these efforts, however, has largely been on women. More study is needed on the epidemiology of trichomoniasis in men as well as how to best diagnose and treat infected men, particularly given its high prevalence and communicability.[9] New molecular technologies have the potential to shift the paradigm of how clinicians detect STIs such as trichomoniasis. Among these, nucleic acid amplification tests have emerged as a more reliable method of detecting *T. vaginalis* when compared with standard wet mount and culture tests. Improving diagnosis through the routine use of such molecular diagnostics would promote better health outcomes for patients who might otherwise go undiagnosed and would provide more accurate prevalence estimates to health system decision makers. In turn, more accurate prevalence estimates might support mandatory reporting of trichomoniasis cases, enabling policymakers to better gauge and address the public health implications of this infection.[23]

Challenges with Trichomoniasis

Asymptomatic nature of infection
Reinfection and drug resistance
Not included in routine STI screening
Not a reportable disease
Stigma and misinformation/misconception
Diagnostic challenges
Potential reproductive health risks

Mitigation measures to be adapted by policy makers for Trichomoniasis

Increase awareness and education
Improve screening and diagnosis
Accessible treatment
Practice of safe sex
Behavioral interventions
Integrate care services
Strengthen research and surveillance

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