Diagnostic Challenges and Current Perspectives of Sexually Transmitted Infections: A Literature Review

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Abstract

Background: Sexually transmitted infections (STIs) are among the most prevalent global health concerns, causing significant medical, social, and economic burdens. Despite their high incidence, STIs remain relatively underexplored in research, highlighting the importance of early and sensitive diagnostics.

Methods: A literature search was conducted in PubMed, and Google Scholar. Only English-language studies published between 2005–2025 were included, focusing on diagnostic methods for STIs in humans. International guidelines and recommendations (WHO, CDC, ECDC, NCDC) were also reviewed to ensure global standards.

Results: Currently, nucleic acid amplification tests, particularly PCR-based assays, are regarded as the gold standard due to their high sensitivity and specificity. Studies consistently demonstrate the superiority of PCR in detecting Trichomonas vaginalis, Chlamydia trachomatis, and Neisseria gonorrhoeae. Despite advances in molecular diagnostics and technological progress, effective management of STIs remains significantly constrained; the existing obstacles arise not only from technical limitations but also from social stigma, systemic deficiencies, and challenges in healthcare accessibility.

Conclusion: Molecular diagnostics, especially PCR, represent the modern standard for STI detection and management. However, social stigma, low public awareness, and restricted healthcare access remain major barriers. In Georgia, the lack of reliable epidemiological data further complicates effective management. Comprehensive national studies and the integration of evidence-based diagnostic strategies are essential to improve STI control and public health outcomes. **(TCM-GMJ August 2025; 10 (2): P59-P63)**

Keywords: STI test; STI PCR; Molecular diagnostic; Venerology; Sexually Transmitted Infections.

Introduction

Sexually transmitted infections (STIs) are among the most common infectious diseases worldwide and remain a major public health concern. They create not only medical but also social and economic challenges. Despite their high global incidence and well-recognized burden, STIs are still relatively underrepresented in scientific research (1).

The World Health Organization (WHO) reports that over one million new STI cases occur every day among people aged 15–49 years, with a large proportion of these infections being asymptomatic (2,3).

In 2020, the WHO estimated 374 million new cases of STIs worldwide, caused by four major curable pathogens: chlamydia (129 million), gonorrhea (82 million), syphilis (7.1 million), and trichomoniasis (156 million) (4). According to the European Centre for Disease Prevention and Control (ECDC), 35,391 cases of syphilis were confirmed in 2022. This represents a 34% increase compared with 2021 and a 41% increase compared with 2018 (5).

STIs have a major impact on sexual and reproductive health, with consequences that extend far beyond the initial infection. They are associated with serious complications such as infertility, ectopic pregnancy, preterm birth, stillbirth, neonatal death, endometritis, pelvic inflammatory disease, and cervical cancer (6–8).

In addition, people with gonorrhea or syphilis are also at higher risk of acquiring HIV (9).

STIs have a significant impact on public health, and the epidemiological data reported worldwide are of considerable concern (10).

Economic analyses estimate that in the United States alone, new STI cases generate about 15.9 billion USD in lifetime direct medical costs each year (11). This enormous economic burden highlights the importance of early and accurate diagnostic strategies.

Over time, a large part of research has examined STI diagnostics, addressing the strengths, limitations, and practical use of both traditional and modern methods (12).

This literature review evaluates current diagnostic approaches, comparing their advantages and limitations, and highlights recent studies on the role of molecular diagnostics in routine patient care.

The literature search was conducted across two major scientific databases: PubMed and Google Scholar. Only English-language articles published between **2005** and 2025 were included. The review was limited to human studies that evaluated diagnostic methods for STIs.

Keywords used:"Sexually transmitted infections", "STI diagnostics", "Trichomonas vaginalis PCR", "STI testing", "syphilis", "RPR", "TPHA diagnosis" "STI Urinary testing"

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In addition, we have reviewed data issued by international organizations (e.g., WHO, CDC, ECDC) to ensure that the analysis was based on globally recognized standard.

Literature Review

The development of diagnostic approaches for STIs has a long history, moving from simple clinical observation to advanced molecular technologies (13).

In the early days, diagnosis relied mainly on visible signs and symptoms, which often was often insufficient for establishing accurate and specific diagnoses. The asymptomatic nature of many infections, their vary clinical manifestations, and the frequent presence of co-infections significantly complicated the diagnostic process, leading to misdiagnoses and inadequate treatment (14, 15).

STIs have been present throughout human history. Written sources from ancient Greece and the Roman Empire describe pathologies with clinical manifestations resembling syphilis (16, 17); however, the term "sexually transmitted infections" was introduced much later, only after the mechanisms of disease transmission had been scientifically clarified (18, 19).

In the 15th century, the widespread outbreak of syphilis in Europe caused significant panic, subsequently providing new impetus for the advancement of medicine. For centuries, the diagnosis of syphilis relied on the identification of characteristic ulcers on the skin and mucous membranes, which in most cases appeared only at a late stage, thereby limiting the effectiveness of treatment (17).

In the 19th century, following the confirmation of the bacterial theory by Robert Koch and Louis Pasteur, the identification of STI pathogens became possible (20). Specifically, in 1879, Albert Neisser described Neisseria gonorrhoeae in specimens obtained from infected patients, which laid the foundation for the application of bacteriological diagnostics in the management of STIs (21).

These developments marked the beginning of a new era in diagnostics, paving the way for the integration of microbiological methods into clinical practice. Microscopy—particularly Gram staining—and bacterial culture became established as the standard approaches. However, these methods demonstrated high specificity only when the pathogen was visually recognizable or cultivable, which was not the case for all STIs (for example, trichomoniasis and chlamydia often remained undetected) (22, 23).

At the same time, it should be noted that culture procedures were often labor-intensive, time-consuming, and required specific laboratory conditions, which limited their widespread clinical application. Moreover, the described diagnostic methods were highly dependent on the concentration of the pathogen.

In the first half of the 20th century, significant progress was achieved in the management of STIs — particularly during the periods of the First and Second World Wars, when syphilis and gonorrhea were highly prevalent among military personnel (8,17). During World War I, sexually transmitted infections became a major challenge for the U.S. Army. As a result, soldiers collectively lost nearly seven million days of active duty, and more than ten thousand men were ultimately discharged from service. In the early years of World War II, sexually transmitted diseases continued to pose a serious problem for the armed forces. In response, the War Department launched an extensive program of education and prevention. Among its efforts were the wide distribution of posters that cautioned soldiers and sailors about the risks associated with overly indulgent sexual behavior (Fig.1) (24).

Figure 1: Venereal disease prevention poster, ca. 1940 (Rasnake MS, et al., 2005)

One of the most important milestones in the development of syphilis diagnostics was the introduction of serological testing (25). The initially employed Wassermann reaction (1906) was later replaced by more accurate and reliable methods, such as RPR (Rapid Plasma Reagin) — a rapid screening test, and TPHA (Treponema pallidum Hemagglutination Assay) in 1966 by Takayuki Tomizawa and Shigeo Kasamatsu— a specific confirmatory test that provided greater diagnostic accuracy (26). The implementation of the Wassermann reaction and subsequently RPR/TPHA testing enabled clinicians to distinguish between active and past infections (27).

From this period onward, serology became one of the principal tools in the diagnosis of STIs. Serological testing proved particularly valuable for the diagnosis of chronic and latent cases of STIs (27). However, while RPR is a widely used serological test, it is nonspecific, as it detects antibodies produced in response to Treponema pallidum.

These antibodies, however, may also be generated in other conditions (e.g., pregnancy, tuberculosis, autoimmune disease, or other inflammatory conditions), meaning that the RPR test is not 100% specific(28).

In the 1970s and 1980s, a major breakthrough occurred in the diagnostics of STIs: the development of polymerase chain reaction (PCR) technology, marking the beginning of molecular diagnostics, fundamentally transformed the accuracy and speed of pathogen detection (29). Nucleic acid –based testing methods are characterized by high sensitivity and specificity, enabling the identification of pathogens even from very small sample quantities. The introduction of this technology made it possible to detect pathogens that were previously difficult or impossible to culture (e.g., Chlamydia trachomatis, Mycoplasma genitalium), many of which had often remained clinically undetected (30).

Current Methods in the Diagnosis of STIs

Today, the diagnosis of STIs encompasses several principal methods, which differ in terms of accuracy, speed, and clinical applicability.

Diagnostic methods for STIs:

1. **Microscopy**

Microscopic examination is historically the first and simplest method in the diagnosis of STIs Clinical specimens (e.g., urethral or cervical swabs) are stained using specific techniques, which enhance the visualization of pathogens. Despite its accessibility and low cost, microscopy has limited sensitivity, particularly in cases of asymptomatic bacterial infections with low pathogen load (23).

Accordingly, its main limitations can be outlined as follows:

- Low sensitivity, particularly in asymptomatic infections;
- Specificity highly dependent on the examiner's expertise;
- Inability to simultaneously identify multiple pathogens

2. Culture

Isolation of the pathogen through culture has long been considered the gold standard for certain STIs, particularly for Neisseria gonorrhoeae. This method not only allows confirmation of infection but also enables the determination of antimicrobial susceptibility. However, culture requires considerable time and specific laboratory conditions (12,23)

Accordingly, its main limitations can be outlined as follows:

- Time-consuming procedure;
- Requires specific culture conditions;
- Sensitivity may be reduced if the specimen is improperly collected or if there is a delay in processing

3. Serological tests

Serology plays an important role in the diagnosis of infections such as syphilis, herpes, and HIV. These tests evaluate the immune response of the host to infection. Serological assays are particularly valuable for the detection of latent or chronic infections; however, in some cases, it is not possible to precisely determine the phase of infection. Accordingly, the main limitations can be outlined as follows (28):

- False-positive or false-negative results;
- Difficulty in differentiating the stage of infection;
- Serological response may develop only after a certain interval following infection (the so-called "serological window").

4. Molecular diagnostics

Molecular diagnostic methods, particularly NAATs, are considered the modern gold standard for the detection of STIs (31). This technology, exemplified by the PCR, is characterized by exceptionally high sensitivity and specificity, allowing the identification of infection from minimal amounts of genetic material (32). NAATs Molecular diagnostics are particularly effective in the detection of asymptomatic and subclinical infections, which is critically important for controlling the spread of STIs (32). In addition, NAATs require less invasive sampling. For these reasons, molecular diagnostics represent not only a clinically effective but also a strategically important public health tool in the management of STIs (23). Nevertheless, these methods also have several limitations:

- Relatively high cost;
- Requires specialized equipment and trained personnel;
- In some cases, detection of DNA fragments does not distinguish between viable and non-viable microorganisms.

A review of the literature on STI diagnostics highlights the decisive role of molecular methods in the early detection and management of infections. In the article "Prevalence of Trichomonas Infection in Relation to Human Papillomavirus (HPV) in Pap Smear Samples of Female Patients Referred to Shahid Sadoughi Hospital, Yazd (Iran)", the limited capacity of Pap smear testing for the detection of trichomoniasis is emphasized, along with the superiority of PCR-based methods. Genotyping through PCR enabled more accurate diagnosis of infection, further confirming the advantages of molecular approaches over traditional methods (33).

The study by Herath et al., conducted in Sri Lanka and comparing microscopic examination, culture, and PCR methods for the detection of Trichomonas vaginalis, demonstrated that PCR outperforms the other methods in terms of sensitivity and specificity (7).

Notable findings were reported in a study conducted by Bahreini et al. in Iran, where Trichomonas vaginalis was detected by PCR in 4.86% of urine samples collected from 534 women. The infection was found to be particularly prevalent among the 21–30 and 41–50 year age groups. This study supports the view that PCR testing should be considered a highly sensitive method in the context of preventive screening (34) .

Studies conducted across different geographical and demographic settings demonstrate variability in the prevalence of infection. In South Korea, the prevalence detected by PCR ranges from 3% to 3.3%, whereas microscopy identifies only 0.6% (35). In Brazil, PCR testing of urine samples among young pregnant women revealed a prevalence of 7.7% (36).

Researcher from Division of Infectious Diseases, David Geffen School of Medicine, University of California Los Angeles, CA, USA, Shannon CL and JD Klausner publishing article entitled "The Growing Epidemic of Sexually Transmitted Infections in Adolescents: A Neglected Population" where they are describing increasing rate of STI in adolescents since 2014, between young women and men who have sex with men at particularly high risk. Barriers to STI screening for adolescents include confidentiality concerns and lack of access to health services. In their work they describe that there is no unique recommendation for treatment of youth people and therefore, additional reserch is needed control how well this population is treated (37). Also noteworthy is a 2017 study by Drinkard et al., that aimed to detect extragenital STIs in college students. The study included 4,093 male students. The results showed that with urogenital screening alone the positivity rate for C. trachomatis was 3.1% and 3.7% with risk-based extragenital screening. For N. gonorrhoeae, the rates were 0.7% with urogenital screening alone and 3.3% with risk-based extragenital screening. Accordingly, based on urogenital screening alone, 26.4% of C. trachomatis and 63.2% of N. gonorrhoeae infections would have been missed - this means that without extragenital screening, one in four C. trachomatis infections and one in two N. gonorrhoeae cases would be missed (38). Bottom of Form

However, diagnosing STIs requires not only regular screening with modern and highly effective methods — both from genital and extragenital material — but also determining the specifics of a particular country. An important study conducted in India compared different primers used for PCR-based detection. The findings revealed that accurate selection of primers significantly increases the diagnostic accuracy of the test. This study underscores the importance of tailoring diagnostic strategies to local conditions (32). This is important because infection prevalence patterns, availability and reliability of diagnostic reagents, healthcare system capacity, as well as cultural and social factors differ across settings, all of which can significantly influence the accuracy and effectiveness of STI screening and management.

Conclusion

Despite the significantly improved capabilities of molecular diagnostics and technological progress, the management of STIs continues to face multifaceted challenges. These challenges are linked not only to technical aspects but also to social and structural factors.

One of the main barriers remains the stigma surrounding STIs, which substantially hinders timely healthcare-seeking behavior and patients' willingness to undergo testing. Furthermore, the generally low level of public awareness regarding STIs, their modes of transmission, and the importance of diagnostics complicates the effective implementation of preventive measures. As literature review shows, limited geographic and economic access to healthcare services also represents a significant challenge.

The involvement of unqualified medical personnel further contributes to reduced diagnostic quality, deficiencies in patient communication, and lack of trust.

Additionally, refusal of diagnostic procedures by patients—often associated with the discomfort and fear related to urethral swab collection—deserves attention.

Collectively, these factors lead to undiagnosed or delayed detection of infections, thereby facilitating the wider spread of STIs and an increase in associated complications.

These social and systemic barriers clearly highlight the need for diagnostic methods that are patient-centered, minimally invasive, highly accurate, and simple to administer. In this regard, urine-based molecular tests are increasingly recognized as a promising and practical alternative in STI diagnostics, reducing both physical discomfort and patient-perceived stigma.

Summarizing the evidence, molecular diagnostics, particularly PCR technology, represent the current standard for STI detection. Studies conducted across diverse geographical and clinical contexts have consistently demonstrated the superior sensitivity and specificity of PCR. Nevertheless, the available evidence remains insufficient to conclusively confirm the superiority of urine-based PCR over swab-based testing in STI diagnosis.

It is also noteworthy that, at present, no reliable epidemiological data are available on the prevalence of STIs in Georgia. Moreover, no nationwide studies have been conducted to evaluate the effectiveness of modern diagnostic methods, which could inform evidence-based management strategies. This research gap hinders both the planning of accurate diagnostics and the adaptation of treatment to individual patients.

Accordingly, comprehensive studies are urgently needed in Georgia to assess STI prevalence, diagnostic practices, and patient needs. Such investigations would facilitate the implementation of evidence-based clinical practice and improve the effective management of STIs. Ultimately, timely detection and management of infections not only improve individual patient outcomes but also serve as an important preventive mechanism in terms of public health and health economics.

Morover, future efforts should focus on integrating molecular testing into national screening programs and establishing standardized diagnostic protocols for STI management in Georgia.

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