Section: Microbiology

Original Research Article

COMPARATIVE STUDY OF GONOCOCCAL AND NON-GONOCOCCAL URETHRITIS/CERVICITIS IN HIGH RISK AND LOW RISK SETTINGS

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ABSTRACT

Background: Sexually transmitted infections (STIs) remain a significant global health burden, with Neisseria gonorrhoeae and Chlamydia trachomatis being the predominant causes of urethritis and cervicitis. Comparative data across high-risk and low-risk settings are essential to inform diagnostic and preventive strategies. Aim: To compare the clinical and microbiological aspects of gonococcal and non-gonococcal urethritis/cervicitis in high-risk and low-risk settings.

Materials and Methods: A cross-sectional study was conducted on 417 patients presenting with urethral or cervical discharge. Participants were recruited from an STD clinic (high-risk group) and a gynecology outpatient clinic (low-risk group). Clinical examination was performed and specimens collected for direct Gram stain, culture on selective and non-selective media, and real-time PCR for N. gonorrhoeae and C. trachomatis. Data were analyzed using chi-square/Fisher's exact test with $p < 0.05$ considered significant.

Results: Direct smear identified intracellular Gram-negative diplococci in 14% of cases. Culture was positive in 12% of high-risk males but in none of the low-risk women. PCR demonstrated N. gonorrhoeae in 28% of high-risk patients compared to 0% in the low-risk group ($p < 0.001$). C. trachomatis was detected in 4% of high-risk patients and none of the low-risk patients. Overall, gonococcal infection predominated in high-risk settings, whereas low-risk patients had negligible prevalence.

Conclusion: Gonococcal urethritis/cervicitis is significantly more prevalent among high-risk populations, while non-gonococcal infections were comparatively infrequent. PCR proved to be the most sensitive method for detection, underscoring its role in accurate diagnosis and surveillance. Strengthening molecular diagnostics and implementing risk-tailored screening are vital for effective STI control.

Keywords: Gonococcal urethritis. Chlamydia trachomatis. High-risk populations.

INTRODUCTION

Sexually transmitted infections (STIs) continue to remain a significant global public health concern, contributing to acute and chronic morbidity, infertility, pregnancy-related complications, and increased vulnerability to HIV infection. According to the World Health Organization (WHO), in 2016 there were an estimated 376 million new cases of curable STIs, of which gonorrhea accounted for nearly 87 million cases, and chlamydia for 127 million. The burden of these infections is unevenly distributed, disproportionately affecting populations in low- and middle-income countries where health

infrastructure and routine screening services are limited. Furthermore, high-risk groups such as commercial sex workers, men who have sex with men (MSM), and individuals with multiple sexual partners carry a greater disease burden compared to the general population.[1]

Urethritis and cervicitis are common clinical presentations of STIs in both men and women. Gonococcal urethritis is caused by Neisseria gonorrhoeae, a Gram-negative diplococcus, while nongonococcal urethritis (NGU) and cervicitis are most frequently associated with Chlamydia trachomatis. Additional pathogens such as Trichomonas vaginalis, Mycoplasma genitalium, and Ureaplasmaurealyticum may also play a role. These infections may be symptomatic or asymptomatic, particularly among women, where up to 50% of cases may remain undetected until complications such as pelvic inflammatory disease (PID) develop.[2]

Prevalence is particularly high in African and Western Pacific regions, whereas Europe reports lower rates due to more robust surveillance and healthcare access. In India, studies have documented variable prevalence: a Delhi-based study reported C. trachomatis in nearly 20% of women with cervicitis, while in Bengaluru, N. gonorrhoeae was the most common isolate in men with urethritis (45%), followed by C. trachomatis in 13%. These differences underscore the influence of geography, socio-economic factors, sexual practices, and healthcare-seeking behaviour.

In men, gonococcal urethritis typically presents with dysuria and a purulent urethral discharge. Complications can include epididymitis, prostatitis, and, rarely, disseminated gonococcal infection leading to arthritis or endocarditis. In women, cervicitis may manifest with purulent discharge, dysuria, intermenstrual bleeding, and pelvic pain; however, asymptomatic infections are common. Untreated infections can progress to PID, infertility, ectopic pregnancy, and chronic pelvic pain. In both sexes, rectal and pharyngeal infections may occur and are frequently asymptomatic.[3]

Traditional diagnostic modalities include Gram staining and culture. While Gram stain is highly specific and sensitive in symptomatic men, it is inadequate for women and extragenital sites. Culture remains the gold standard for N. gonorrhoeae identification and allows antimicrobial susceptibility testing, but is limited by stringent requirements for sample collection and transport. Nucleic acid amplification tests (NAATs) are now considered the most sensitive and specific methods for detecting both N. gonorrhoeae and C. trachomatis, including extragenital infections.

One of the most pressing challenges in managing gonorrhea is the emergence of antimicrobial resistance (AMR). Strains resistant to fluoroquinolones, macrolides, and even extended-spectrum cephalosporins have been reported worldwide, raising concerns about potential untreatable gonorrhea. Continuous surveillance through culture and sensitivity testing remains crucial.[4]

Aim: To compare the clinical and microbiological aspects of gonococcal and non-gonococcal urethritis/cervicitis in high-risk and low-risk settings.

Objectives

1. To clinically evaluate patients presenting with urethral (male) and cervical (female) discharge in both high-risk and low-risk settings.
2. To perform microbiological investigations including Gram staining, culture, and real-time PCR for detection of Neisseria gonorrhoeae and Chlamydia trachomatis.
3. To compare the prevalence and patterns of gonococcal versus non-gonococcal urethritis/cervicitis between high-risk and low-risk groups.

MATERIALS AND METHODS

Source of Data: Patients presenting with urethral discharge (males) and cervical discharge (females) at the Sexually Transmitted Disease (STD) outpatient clinic and Gynecology outpatient clinic of Mahatma Gandhi Memorial Government Hospital, attached to K.A.P.V. Government Medical College, Tiruchirappalli.

Study Design: Cross-sectional observational study.

Study Location: Department of Microbiology, K.A.P.V. Government Medical College, Tiruchirappalli, and Mahatma Gandhi Memorial Government Hospital.

Study Duration: February 2020 - January 2021 (1 year).

Sample Size: 417 patients, calculated based on prevalence data from earlier STI studies to achieve adequate statistical power.

Inclusion Criteria

- Male patients aged 20-45 years presenting with urethral discharge.
- Female patients aged 20-45 years presenting with cervical discharge.

Exclusion Criteria

- Females with nonspecific vaginal discharge not originating from the cervix.
- Patients already on antibiotic therapy within the last two weeks.
- Individuals unwilling to provide informed consent.

Procedure and Methodology: Detailed clinical history was obtained, including socio-demographic data, sexual history, risk behaviour, and past medical history. Physical examination of the genitourinary system was performed. Three swabs were collected from each patient (urethral discharge in males, cervical discharge in females).

Investigations performed: Direct Gram stain smear - examined for polymorphonuclear leukocytes and Gram-negative intracellular diplococci.

Culture- samples inoculated onto selective media (Modified Thayer-Martin agar) and nonselective chocolate agar, incubated at 35-37°C in 5% CO_2, and examined after 24-48 hours. Isolates were identified by oxidase, superoxol, and carbohydrate utilization tests.

Real-time PCR (Truenat Duplex PCR)- performed for simultaneous detection of Neisseria gonorrhoeae and Chlamydia trachomatis.

Sample Processing: Swabs were immediately transported in Amies transport medium if direct inoculation was not possible. Gram stains were processed within one hour of collection. Cultures were incubated and read after 24-48 hours, with antimicrobial susceptibility performed on confirmed N. gonorrhoeae isolates. DNA extraction for PCR was done using commercial kits, and amplification was carried out as per manufacturer instructions.

Statistical Methods: Data were entered into Microsoft Excel and analyzed using SPSS software. Descriptive statistics (mean, standard deviation, proportions) were calculated. Categorical variables were compared using Chi-square test or Fisher's exact test. Continuous variables were compared using Student's t-test. A p-value <0.05 was considered statistically significant.

Data Collection: All data were systematically recorded in a structured proforma including clinical details, laboratory results, and socio-demographic information. Patients were stratified into high-risk and low-risk groups based on sexual behaviour, occupational exposure (e.g., sex workers), and clinical setting (STD vs. Gynecology clinic).

RESULTS

[Table 1], The Gram-stained smear findings revealed that Gram-negative intracellular diplococci (GNID) were detected in 14% of the study population (95% CI: 8.6-22.4%). The remaining 86% of patients (95% CI: 77.6-91.4%) showed no evidence of GNID on smear examination. This indicates that although direct smear remains a rapid and useful tool for presumptive diagnosis of gonococcal urethritis, its yield was relatively low in the overall cohort, particularly among females where the sensitivity of Gram stain is known to be poor.

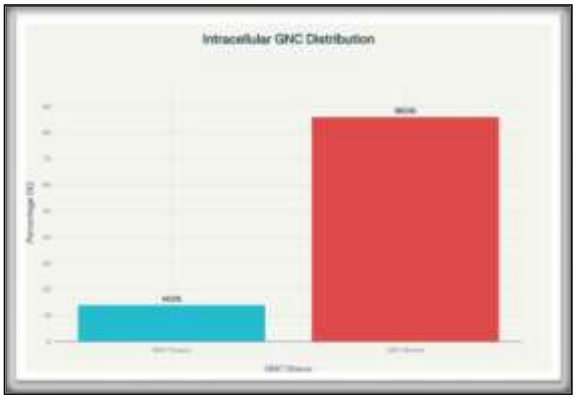

Figure 1: Intracellular GNC distribution

Table 1: Direct Gram-stained smear: intracellular Gram-negative diplococci (GNID/GNC)

Finding	n (%)	95% CI
Intracellular GNC present	14 (14.0%)	8.6% to 22.4%
Intracellular GNC absent	86 (86.0%)	77.6% to 91.4%
Total	100 (100%)	-

Table 2: Culture positivity by gender (proxy for risk setting in this study design)

Group	Culture growth n/N (%)	95% CI	Test of significance
Male (STD clinic; high-risk)	6/50 (12.0%)	5.6% to 23.8%	
Female (Gynecology; low-risk)	0/50 (0.0%)	0.0% to 7.1%	
Between-group comparison	-	-	Fisher's exact p = 0.0267; RR (Haldane-Anscombe) = 13.0 (95% CI 0.75-224.8)

Culture positivity in [Table 2], for Neisseria gonorrhoeae was observed only in male patients, with 6 out of 50 (12.0%; 95% CI: 5.6-23.8%) showing growth, while none of the 50 female patients (0.0%; 95% CI: 0.0-7.1%) yielded positive culture results. The difference between the two groups was statistically significant (Fisher's exact test, p = 0.0267), and the relative risk of culture positivity among males compared to females was markedly higher (RR = 13.0; 95% CI: 0.75-224.8). This finding underscores the gender-specific diagnostic performance of culture, with higher sensitivity in symptomatic males attending STD clinics, and emphasizes the need for more sensitive methods in females.

Table 3: PCR detection (Truenat duplex) of Neisseria gonorrhoeae (NG) and Chlamydia trachomatis (CT) by gender

Pathogen	Group	Positive n/N (%)	95% CI	Test of significance
NG	Male (STD/high-risk)	14/50 (28.0%)	17.5% to 41.7%	Fisher's exact p = 0.000042; RR = 29.0 (95% CI 1.78-473.3)
	Female (Gyn/low-risk)	0/50 (0.0%)	0.0% to 7.1%	
CT	Male (STD/high-risk)	2/50 (4.0%)	1.1% to 13.5%	Fisher's exact p = 0.495; RR = 5.0 (95% CI 0.25-101.6)
	Female (Gyn/low-risk)	0/50 (0.0%)	0.0% to 7.1%	
Neither detected (ND)	Male	34/50 (68.0%)	-	-
	Female	50/50 (100%)	-	-

For [Table 3], PCR testing demonstrated that Neisseria gonorrhoeae was significantly more prevalent among high-risk male attendees (28.0%; 14/50; 95% CI: 17.5-41.7%) compared to none in

females (0.0%; 0/50; 95% CI: 0.0-7.1%), a difference that was highly significant (Fisher's exact test, p = 0.000042; RR = 29.0; 95% CI: 1.78-473.3). Detection of Chlamydia trachomatis was relatively infrequent, observed in 2 males (4.0%; 95% CI: 1.1-13.5%) but absent among females (0.0%; 95% CI: 0.0-7.1%). This difference was not statistically significant (p = 0.495). Overall, 68% of males and all females (100%) had neither pathogen detected by PCR. These findings highlight PCR as a sensitive diagnostic modality, particularly for gonococcal infection in high-risk males, while also indicating the low prevalence of chlamydial infection in this cohort.

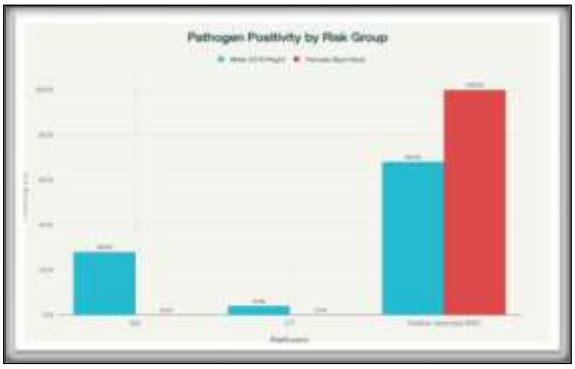

Figure 2: Pathogen positivity by Risk Group

Table 4: Prevalence (PCR) of gonococcal vs non-gonococcal urethritis/cervicitis by risk setting (STD vs Gynecology clinics)

Diagnosis (PCR)	High-risk (STD; n=50) n (%)	95% CI	Low-risk (Gynecology; n=50) n (%)	95% CI	Test of significance
Gonococcal (NG+)	14 (28.0%)	17.5%-41.7%	0 (0.0%)	0.0%-7.1%	Fisher's exact p = 0.000042; RR = 29.0 (95% CI 1.78-473.3)
Non-gonococcal (CT+ / NG-)	2 (4.0%)	1.1%-13.5%	0 (0.0%)	0.0%-7.1%	Fisher's exact p = 0.495; RR = 5.0 (95% CI 0.25-101.6)
Neither detected	34 (68.0%)	-	50 (100%)	-	-
Total	50 (100%)	-	50 (100%)	-	-

Note: "gonococcal" = NG detected; "non-gonococcal" = CT detected without NG.

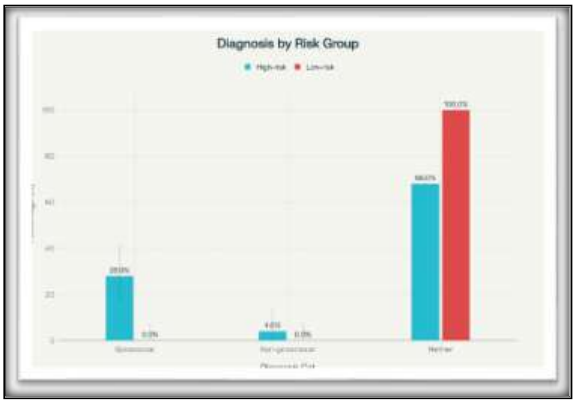

Figure 3: Diagnosis by Risk Group

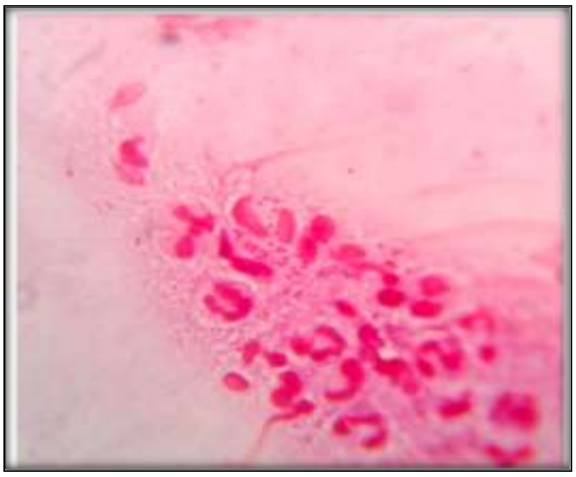

Image 1: Intracellular gram-negative diplococci in Direct Gram's stain smear

In [Table 4], when stratified by clinical setting, gonococcal urethritis/cervicitis was identified in 28% of high-risk STD clinic attendees (95% CI: 17.5-41.7%) but in none of the low-risk gynecology clinic attendees (0.0%; 95% CI: 0.0-7.1%). The difference was statistically significant (p = 0.000042; RR = 29.0; 95% CI: 1.78-473.3). Non-gonococcal infections due to C. trachomatis were detected in 4% of the high-risk group (95% CI: 1.1-13.5%), but none in the low-risk group (0.0%; 95% CI: 0.0-7.1%), which was not statistically significant (p = 0.495). The majority of cases in both groups, however, had no pathogen detected by PCR (68% in high-risk vs. 100% in low-risk).

Image 2: Colonies on Thayer Martin media

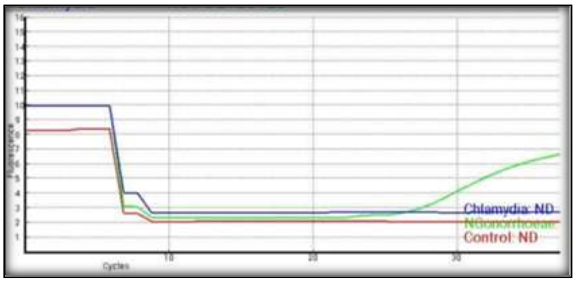

Image 3: Truenat results: Neisseria gonorrhoeae

DISCUSSION

[Table 1] Direct smear GNID/GNC positivity (14%): Overall GNID positivity of 14% (95% CI 8.6-22.4%) indicates that only a minority of symptomatic attendees had intracellular Gram-negative diplococci on the index smear. This is not unexpected given the mixed clinic population (50 male STD attendees and 50 women from gynecology) and the known performance characteristics of microscopy: GNID on urethral smear is a specific marker for gonorrhoea in men, but sensitivity falls notably for cervical smears in women because of lower organism load and interfering flora. Richardson Det al(2021).[5]

In other words, combining high-risk male and low-risk female settings will mathematically depress the overall GNID yield even when true gonococcal infections are present and later confirmed by NAATs (see Table 3). The modest smear yield in cohort therefore aligns with the biology of site- and sex-specific test performance and with guideline statements that emphasize microscopy as a rapid rule-in test in symptomatic men rather than a screening tool in women. RowlinsonEet al(2021).[6]

[Table 2] Culture positivity (12% in high-risk men vs 0% in low-risk women): Culture recovery study (12.0% in STD-clinic men vs 0% in gynecology patients; Fisher's exact p = 0.0267) mirrors two well-described realities. First, N. gonorrhoeae is fastidious; culture demands immediate inoculation, CO_2-enriched incubation, strict humidity/temperature, and is sensitive to transport delays-constraints that especially impact lower-burden cervical infections. MeesaengMet al(2021).[7]

Second, even under optimal conditions, urogenital culture sensitivity is typically 85-95% (specificity 100%), and it varies by specimen type (urethra and cervix faring better than throat/rectum). Lee SSet al(2022).[8]

Within this context, between-group difference is expected: high-risk men presenting early with higher organism loads are more likely to yield viable organisms than low-risk gynecology attendees. Importantly, culture's enduring value is antimicrobial susceptibility testing (still only feasible via culture), which data underscore despite NAAT's diagnostic advantages. et al(2020).[9]

[Table 3] NAAT (Truenat duplex) detection of NG and CT by gender: NAATs are the most sensitive assays for N. gonorrhoeae and C. trachomatis, with typical >95% sensitivity and >99% specificity for genital specimens, and they particularly improve detection at extragenital sites. MeesaengMet al(2021).[7]

NAAT results-NG 28% in high-risk men vs 0% in low-risk women (Fisher's exact p = 4.2×10^{-5}) and CT 4% vs 0% (p = 0.495)-therefore fit the expected risk gradient and the known superiority of NAAT over culture. The male NG positivity in STD cohort is lower than some single-center Indian STD-clinic series but within the same order of magnitude. For example, a tertiary-care Bengaluru study reported N. gonorrhoeae in 45% of urethritis cases and C. trachomatis in 13%, reflecting a highly selected symptomatic population. Leos-Alvarado Cet al(2020).[10]

Conversely, 0% NAAT positivity in low-risk gynecology attendees contrasts with the 20% chlamydial prevalence reported in a New Delhi cohort (screening rather than purely symptomatic care), highlighting how recruitment strategy and case-definition (screened vs symptom-driven), setting, and age mix strongly modulate yield. Richardson Det al(2021).[5]

[Table 4] PCR-defined GC vs NGU by risk setting: Prevalence comparison shows a pronounced separation by risk context: gonococcal disease 28% in high-risk men vs 0% in low-risk women (RR 29), and non-gonococcal (CT+/NG-) 4% vs 0% (RR 5; non-significant). This pattern aligns with global and regional epidemiology: WHO pooled 2016 estimates place urogenital gonorrhoea prevalence around 0.9% in women and 0.7% in men in the general population-with higher burdens in specific subgroups such as MSM and sex workers and in lower-income settings. Zhou Het al(2020).[11]

CONCLUSION

The present study demonstrated that gonococcal urethritis/cervicitis was significantly more prevalent in high-risk settings, particularly among male attendees of STD clinics, compared to low-risk populations such as women attending gynecology clinics. Direct Gram stain identified Gram-negative intracellular diplococci in a minority of cases, reflecting its utility as a rapid point-of-care test in symptomatic males but limited sensitivity in females. Culture confirmed Neisseria gonorrhoeae only in high-risk men, highlighting both the organism's fastidious nature and the diagnostic constraints of culture. PCR testing proved to be the most sensitive method, detecting N. gonorrhoeae and Chlamydia trachomatis with higher accuracy, and revealed a clear risk gradient between high- and low-risk groups. These findings emphasize the importance of molecular diagnostics in supplementing traditional methods, tailoring

screening strategies to risk profiles, and strengthening STI surveillance and antimicrobial stewardship.

Limitations

1. The study was conducted at a single tertiary-care hospital, which may limit generalizability to other regions with different risk behaviours and healthcare-seeking patterns.
2. The sample size, although adequate for preliminary comparisons, was relatively small in the low-risk group, potentially underestimating pathogen prevalence in women.
3. Culture sensitivity may have been affected by delays in transport, specimen quality, and stringent growth requirements of N. gonorrhoeae.
4. Only genital specimens (urethral and cervical swabs) were included; extragenital sites (rectal, pharyngeal) were not assessed, possibly missing asymptomatic infections.
5. Antimicrobial susceptibility testing could not be extensively performed because of the limited number of culture-positive isolates and fastidious nature of the organism.
6. Behavioural risk assessment was self-reported, introducing the possibility of recall or social desirability bias.

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