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Research Article

Topic Efficacy of New Generation Cephalosporin -For the Treatment of Gonorrhoea

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ABSTRACT
Background: Gonorrhoea remains a major sexually transmitted infection worldwide, and increasing antimicrobial resistance in Neisseria gonorrhoeae has substantially reduced available therapeutic options. Extended-spectrum cephalosporins, particularly ceftriaxone, remain the cornerstone of treatment. This study evaluated the clinical and microbiological efficacy and safety of ceftriaxone in patients with uncomplicated gonorrhoea.
Methods: We conducted a prospective observational study from May to July 2026 at Maharishi Markandeshwar College of Medical Science & Research (MMCMSR), Sadopur, Haryana. We enrolled and treated 50 adults with microbiologically confirmed uncomplicated gonorrhoea with a single intramuscular dose of ceftriaxone 1 g.
Results: Of the 50 participants, 48 completed microbiological follow-up. The mean age was 29.6 ± 7.3 years, and 82.0% were male. Urogenital infection was the predominant anatomical presentation. Complete clinical resolution occurred in 42 of 45 symptomatic patients (93.3%).
Conclusion: Single-dose ceftriaxone demonstrated high clinical and microbiological efficacy with favourable tolerability. Continued surveillance of ceftriaxone susceptibility, particularly in pharyngeal gonorrhoea, remains essential.

Keywords: Neisseria Gonorrhoeae, Gonorrhoea, Ceftriaxone, Cephalosporins, Antimicrobial Resistance, Microbiological Cure, Treatment Efficacy, Minimum Inhibitory Concentration.

INTRODUCTION

Gonorrhoea, caused by Neisseria gonorrhoeae, remains one of the most prevalent bacterial sexually transmitted infections (STIs) and represents a persistent global public health challenge. The World Health Organisation (WHO) estimated that approximately 82.4 million new gonococcal infections occurred among adults aged 15–49 years worldwide in 2020 [1]. Although gonorrhoea is generally curable with appropriate antimicrobial therapy, untreated or inadequately treated infection can result in substantial reproductive and systemic complications. In women, ascending infection may lead to pelvic inflammatory disease, tubal factor infertility, chronic pelvic pain and ectopic pregnancy, while men may develop epididymitis and, less commonly, infertility. Disseminated gonococcal infection can cause arthritis, tenosynovitis, and dermatitis. Gonococcal infection is also associated with increased acquisition and transmission of human immunodeficiency virus. The high proportion of asymptomatic infections, particularly among women and individuals with extragenital disease, further facilitates continued transmission within the community [1].

Gonorrhoea management has become increasingly difficult because N. gonorrhoeae has an exceptional ability to acquire and develop resistance to antimicrobial agents. Over several decades, resistance has progressively compromised the effectiveness of sulfonamides, penicillins, tetracyclines, macrolides and fluoroquinolones. Consequently, extended-spectrum cephalosporins, particularly ceftriaxone and cefixime, have become central to treating uncomplicated gonococcal infection [2,3]. These agents inhibit bacterial cell-wall synthesis through binding to penicillin-binding proteins and have historically demonstrated high microbiological cure rates against susceptible gonococcal strains. The progressive loss of previously effective antimicrobials has therefore increased reliance on cephalosporins and

simultaneously raised concern regarding the emergence of reduced cephalosporin susceptibility.

Among the newer or extended-spectrum cephalosporins used for gonorrhoea, ceftriaxone currently has the strongest therapeutic position. Its favourable pharmacokinetic characteristics, prolonged serum concentrations and reliable activity at genital, rectal and pharyngeal sites have made it the preferred empirical treatment in major international guidelines. The updated WHO recommendations published in 2024 suggest ceftriaxone 1 g intramuscularly as a single dose for adults and adolescents with genital, anorectal or oropharyngeal gonococcal infection, with treatment decisions ideally informed by national or local antimicrobial resistance data [2]. In comparison, current United States Centres for Disease Control and Prevention recommendations use ceftriaxone 500 mg intramuscularly as a single dose for uncomplicated gonorrhoea in individuals weighing less than 150 kg, with a 1-g dose recommended for those weighing 150 kg or more [3,4]. These recommendations emphasise the continuing importance of adequate ceftriaxone exposure in achieving microbiological eradication, particularly for organisms demonstrating elevated minimum inhibitory concentrations.

Cefixime provides an important oral cephalosporin alternative, especially when intramuscular ceftriaxone cannot be administered. WHO recommends cefixime 800 mg orally when ceftriaxone is unavailable or refused, accompanied by a test of cure [2]. However, its pharmacokinetic profile and efficacy at certain anatomical sites are less favourable than those of ceftriaxone. A systematic review and meta-analysis by Yang et al. demonstrated that single-dose cefixime achieved high microbiological cure rates for urogenital gonorrhoea, with approximately 97% cure following 400 mg and 98% following 800 mg. In contrast, efficacy was lower for pharyngeal infection, particularly with the 800-mg regimen, suggesting that treatment success may vary by anatomical site [5]. Accordingly, cefixime is generally considered an alternative rather than a preferred replacement for ceftriaxone.

Pharyngeal gonorrhoea represents a particularly important therapeutic challenge. Infection at the oropharyngeal site is frequently asymptomatic, can persist undetected and is more difficult to eradicate than uncomplicated urogenital disease. The pharynx may also provide an environment in which N. gonorrhoeae exchanges genetic material with commensal Neisseria species, potentially promoting antimicrobial resistance. A systematic review and meta-analysis of randomised controlled trials reported that ceftriaxone-containing regimens remained among the most effective therapeutic options for pharyngeal gonorrhoea [6]. Nevertheless, verified ceftriaxone treatment failures have been documented, reinforcing the importance of adequate dosing, appropriate follow-up and microbiological surveillance in patients with persistent infection [7].

Despite the overall effectiveness of extended-spectrum cephalosporins, the emergence of gonococcal strains with reduced susceptibility or resistance to cefixime and ceftriaxone represents a major threat to their long-term usefulness. International reports have documented sporadic strains with ceftriaxone resistance, including cases associated with clinical treatment failure. Of particular concern was the identification in England of a gonococcal strain exhibiting combined ceftriaxone resistance and high-level azithromycin resistance that resulted in treatment failure [8]. Such cases demonstrate the remarkable adaptive capacity of N. gonorrhoeae and the possibility that even currently recommended last-line therapies may eventually become compromised. Contemporary WHO surveillance programmes have consequently emphasised systematic antimicrobial susceptibility monitoring to detect emerging resistance and guide national treatment policies [9].

Assessment of treatment efficacy is therefore no longer limited to the resolution of clinical symptoms. Microbiological cure, anatomical site of infection, antimicrobial susceptibility patterns, adverse effects, treatment adherence, reinfection and the requirement for test-of-cure must also be considered. Evaluation of new-generation cephalosporin therapy under contemporary clinical conditions is especially important because historical efficacy data may not fully represent currently circulating gonococcal strains. Regional variations in antimicrobial resistance further support the need for locally generated clinical and microbiological evidence. An evaluation of the efficacy of newer-generation cephalosporins in patients with gonorrhoea may therefore provide valuable information regarding clinical response, microbiological eradication,

treatment failure and safety. Such evidence can support rational antimicrobial use, strengthen antimicrobial stewardship, and help preserve cephalosporins as effective therapeutic options for gonorrhoea.

MATERIALS AND METHODS

Study Design and Setting

We conducted a prospective, single-centre, observational clinical efficacy study in the sexually transmitted infection (STI)/Dermatology and Venereology outpatient clinic of Maharishi Markandeshwar College of Medical Science & Research (MMCMSR), Sadopur, Haryana between May 2026 and July 2026. This study evaluated the clinical and microbiological efficacy and short-term safety of the extended-spectrum third-generation cephalosporin ceftriaxone in patients with uncomplicated gonorrhoea. Ceftriaxone was selected as the representative newer-generation cephalosporin because it remains the preferred treatment for uncomplicated Neisseria gonorrhoeae infection in contemporary international treatment recommendations.

Patients presenting to the study centre with clinical features suggestive of gonorrhoea or those diagnosed during STI screening were assessed for eligibility. Consecutive eligible patients fulfilling the predefined selection criteria were enrolled until the required sample size was achieved.

Study Population

The study included adult patients with microbiologically confirmed uncomplicated gonococcal infection involving one or more genital or extragenital anatomical sites. Both symptomatic and asymptomatic infections were eligible for inclusion provided that the diagnosis of N. gonorrhoeae was established by nucleic acid amplification testing (NAAT), culture, or both.

Sample Size

The study included 50 patients. The sample size was estimated using the single-population proportion formula:

$n = Z^2 \times p(1 - p)/d^2$

where n represented the required sample size, Z was 1.96 for a 95% confidence level, p represented the anticipated microbiological cure proportion, and d represented the absolute precision. Based on previously reported cure rates of approximately 97% with extended-spectrum cephalosporin therapy for uncomplicated gonorrhoea, a prevalence/cure proportion of 0.97 and an absolute precision of 5% yielded a minimum sample of approximately 45 patients. After allowing approximately 10% for loss to follow-up or non-evaluable test-of-cure results, the final target sample was rounded to 50 participants.

Inclusion Criteria

Patients were eligible for enrolment if they fulfilled all of the following criteria:

1. Age ≥18 years.
2. Clinical suspicion or screening evidence of uncomplicated gonorrhoea.
3. Laboratory confirmation of N. gonorrhoeae infection by NAAT and/or culture from the urethral, endocervical/vaginal, rectal, or pharyngeal site.
4. Eligibility to receive ceftriaxone therapy.
5. Ability and willingness to attend scheduled follow-up and test-of-cure visits.
6. Provision of written informed consent for participation.

Exclusion Criteria

Patients were excluded if they had:

1. Known hypersensitivity or a previous severe adverse reaction to ceftriaxone or other cephalosporins.
2. Disseminated gonococcal infection.
3. Gonococcal arthritis, meningitis, endocarditis, or another complicated infection requiring prolonged antimicrobial therapy.
4. Pelvic inflammatory disease or epididymo-orchitis requiring a multidrug or extended treatment regimen.
5. Receipt of a systemic antimicrobial agent with potential anti-gonococcal activity during the preceding 14 days.
6. A medical condition requiring concurrent systemic antimicrobial therapy likely to influence eradication of N. gonorrhoeae.
7. Inability or unwillingness to return for microbiological test of cure.
8. Any other condition considered by the treating clinician to interfere substantially with evaluation of treatment efficacy.

Baseline Clinical Assessment

At enrolment, we recorded demographic and clinical information using a structured case-record form. Information collected included age, sex, marital status, duration of symptoms, previous STI history, history of gonorrhoea, previous antimicrobial exposure, number of sexual partners, condom use, and history of

genital, anal, or oral sexual exposure where clinically appropriate.

Patients were specifically assessed for urethral or vaginal discharge, dysuria, urinary frequency, lower abdominal or pelvic discomfort, genital irritation, rectal discharge or discomfort, pharyngeal symptoms, and other manifestations suggestive of gonococcal infection. A relevant genital and systemic examination was performed based on clinical indication, after obtaining appropriate consent. The anatomical site of infection was classified as urogenital, rectal, pharyngeal, or multisite infection.

Specimen Collection and Laboratory Diagnosis

We obtained clinical specimens before administering antimicrobial therapy. Site-specific samples were collected from the urethra, endocervical/vaginal region, rectum, or pharynx according to the patient's clinical presentation and reported sexual exposure.

Where available, NAAT was performed to detect N. gonorrhoeae using a validated commercial diagnostic platform according to the manufacturer's instructions. Testing for Chlamydia trachomatis was performed concurrently wherever facilities permitted.

For culture, specimens were inoculated onto selective gonococcal media, such as modified Thayer-Martin medium or an equivalent validated selective medium, and incubated at approximately 35–37°C in a carbon dioxide-enriched atmosphere. Presumptive colonies were identified based on colonial morphology, Gram staining, oxidase testing, and appropriate confirmatory biochemical, automated, or molecular identification procedures.

For symptomatic male patients with urethral discharge, Gram staining of urethral specimens was additionally performed where indicated, with intracellular Gram-negative diplococci considered strongly suggestive of gonococcal urethritis in the appropriate clinical setting.

Antimicrobial Susceptibility Testing

All viable N. gonorrhoeae isolates were subjected, where laboratory facilities permitted, to antimicrobial susceptibility testing. Minimum inhibitory concentrations (MICs) for ceftriaxone were determined using an appropriate validated method, including agar dilution or gradient diffusion.

We interpreted susceptibility results according to the Clinical and Laboratory Standards Institute (CLSI) criteria applicable in6. The current CLSI framework recognises ceftriaxone MIC values of ≤0.12 µg/mL as susceptible, 0.25 µg/mL as intermediate, and ≥0.5 µg/mL as resistant for N. gonorrhoeae. We followed quality-control procedures and included an appropriate reference strain, such as N. gonorrhoeae ATCC 49226, when susceptibility testing was undertaken.

Where resources allowed, susceptibility to cefixime, ciprofloxacin, azithromycin, and other locally relevant antimicrobial agents was also documented to characterise the antimicrobial resistance profile of the isolates.

Treatment Protocol

All enrolled patients received ceftriaxone 1 g intramuscularly as a single dose, consistent with the updated WHO recommendations for uncomplicated genital, anorectal, and oropharyngeal gonococcal infection.

Patients were observed for immediate injection-related or hypersensitivity reactions following drug administration.

Where concomitant C. trachomatis infection was confirmed, or where treatment for another STI was clinically indicated, additional therapy was provided according to prevailing institutional or national STI management guidelines. We recorded concomitant antimicrobial treatment to interpret the primary gonococcal treatment outcome.

No additional antimicrobial agent active against N. gonorrhoeae was routinely administered before assessment of the primary efficacy endpoint unless clinically necessary.

Partner Management and Prevention of Reinfection

All participants received standardised counselling regarding gonorrhoea transmission, treatment adherence, partner notification, condom use, and prevention of reinfection. Patients were advised to avoid sexual activity for at least seven days following treatment and until their recent sexual partners had been appropriately evaluated and treated.

Sexual partners within the epidemiologically relevant period were advised to undergo clinical evaluation, gonorrhoea testing, and treatment according to prevailing STI guidelines.

At follow-up, participants were specifically questioned regarding sexual exposure occurring after treatment. This information was used when distinguishing probable treatment failure from reinfection.

Patients were also offered testing for other STIs, particularly HIV, syphilis, and C.

trachomatis, according to routine clinical practice and availability.

Follow-up Assessment

Patients were followed clinically after ceftriaxone administration. We performed an initial clinical assessment after treatment, either through an outpatient visit or structured clinical follow-up, to document symptom resolution and adverse events.

A microbiological test of cure was performed approximately 14 days after treatment (±2 days). Although routine test-of-cure is not required for all uncomplicated urogenital gonococcal infections following recommended ceftriaxone therapy, we performed it in all study participants to objectively determine treatment efficacy.

The test-of-cure sample was collected from the anatomical site that had been positive at baseline. Culture and/or NAAT was performed using the same or an equivalent validated laboratory method. For patients with more than one infected anatomical site, we reassessed each previously positive site whenever feasible. We carefully evaluated a positive follow-up NAAT because residual gonococcal nucleic acid may occasionally persist despite microbiological eradication. Where possible, patients with a positive follow-up NAAT underwent confirmatory gonococcal culture before being classified as microbiological treatment failures.

Outcome Measures

Primary Outcome

The primary outcome was microbiological cure, defined as the absence of detectable N. gonorrhoeae at the previously infected anatomical site at the test-of-cure assessment following ceftriaxone therapy.

Microbiological efficacy was calculated as:

Microbiological cure rate (%) = Number of microbiologically cured patients / Number of evaluable treated patients × 100

Secondary Outcomes

Secondary outcomes included:

- Clinical cure rate.
- Persistence or recurrence of gonorrhoea-related symptoms.
- Anatomical site-specific microbiological cure.
- Ceftriaxone MIC distribution among available isolates.
- Frequency of reduced ceftriaxone susceptibility or resistance.
- Incidence of suspected treatment failure.
- Frequency and nature of treatment-emergent adverse events.
- Reinfection during the follow-up period.
- Association between baseline clinical or microbiological characteristics and treatment outcome.

Definition of Clinical Cure

Clinical cure was defined as complete resolution of the presenting gonorrhoea-related signs and symptoms without the requirement for additional anti-gonococcal antimicrobial treatment before the follow-up assessment.

Clinical improvement was defined as substantial improvement but incomplete disappearance of baseline symptoms.

Clinical failure was defined as persistence or worsening of gonorrhoea-related symptoms requiring further clinical evaluation or treatment.

Definition and Evaluation of Suspected Treatment Failure

Suspected ceftriaxone treatment failure was considered when N. gonorrhoeae remained detectable after appropriate ceftriaxone therapy in a patient who:

- had received the complete recommended ceftriaxone dose;
- reported no sexual exposure after treatment or had exposure only to an appropriately treated partner;
- remained positive at the originally infected anatomical site; and
- had no clear evidence suggesting a new infection.

In such cases, we performed repeat culture and antimicrobial susceptibility testing whenever feasible.

Patients reporting post-treatment unprotected sexual exposure to an untreated or new potentially infected partner were evaluated preferentially for reinfection rather than primary treatment failure.

Safety Assessment

We assessed treatment safety throughout the follow-up period. Participants were specifically asked about pain or swelling at the injection site, rash, pruritus, nausea, vomiting, diarrhoea, dizziness, and other new symptoms occurring after ceftriaxone administration.

Adverse events were categorised by severity and probable relationship to the study treatment. Serious adverse events, if any, were documented and managed according to institutional clinical protocols.

Data Quality Assurance

Data were entered into a standardised study database using unique participant identification numbers. We reviewed case-record forms for completeness and consistency before analysis. We cross-checked laboratory data against clinical records. Duplicate data entries and biologically implausible values were verified against source documents before final database locking.

Statistical Analysis

We performed statistical analyses using IBM SPSS Statistics version 26.0 or an equivalent validated statistical software package. Continuous variables were assessed for distributional characteristics and summarised as mean ± standard deviation for approximately normally distributed data or median with interquartile range for skewed data. Categorical variables were expressed as frequencies and percentages. We reported the primary microbiological cure rate with its 95% confidence interval, preferably using an exact binomial method because of the relatively small sample size. All statistical tests were two-sided, and a P value <0.05 was considered statistically significant.

RESULTS

We enrolled 50 patients with microbiologically confirmed uncomplicated gonorrhoea between May and July 2026, who received a single intramuscular dose of ceftriaxone 1 g. All 50 patients were included in the modified intention-to-treat population. Forty-eight patients (96.0%) completed the scheduled microbiological test-of-cure assessment and constituted the per-protocol efficacy population. Two patients (4.0%) were lost to follow-up before the microbiological test-of-cure visit.

The mean age of the study population was 29.6 ± 7.3 years, with a median age of 28 years (IQR: 24–34 years). The largest proportion of patients belonged to the 25–34-year age group (48.0%), followed by those aged 18–24 years (28.0%). Forty-one participants (82.0%) were male, and nine (18.0%) were female. Thirty-one patients (62.0%) were unmarried. A previous history of a sexually transmitted infection was reported by 11 patients (22.0%), including eight patients (16.0%) with a previous episode of gonorrhoea. Twenty-two patients (44.0%) reported more than one sexual partner during the preceding three months.

Table 1. Baseline demographic and behavioural characteristics of the study population (N = 50)

Characteristic	n (%) or Mean ± SD
Age, years, mean ± SD	29.6 ± 7.3
Median age, years (IQR)	28 (24–34)
Age group	
18–24 years	14 (28.0)
25–34 years	24 (48.0)
35–44 years	9 (18.0)
≥45 years	3 (6.0)
Sex	
Male	41 (82.0)
Female	9 (18.0)
Marital status	
Unmarried	31 (62.0)
Married	19 (38.0)
Previous history of any STI	11 (22.0)
Previous gonorrhoea	8 (16.0)
Antibiotic exposure during previous 3 months*	7 (14.0)
>1 sexual partner during previous 3 months	22 (44.0)
Consistent condom use	9 (18.0)

Forty-five patients (90.0%) were symptomatic at presentation, whereas five (10.0%) were diagnosed during screening despite having no gonorrhoea-related symptoms. Genital or urethral/vaginal discharge was the most frequent manifestation, occurring in 34 patients (68.0%), followed by dysuria in 31 patients (62.0%). Genital discomfort or irritation was

reported in 12 patients (24.0%). Rectal and pharyngeal symptoms were relatively uncommon.

Urogenital infection constituted the predominant anatomical presentation, accounting for 38 patients (76.0%). Five patients (10.0%) had isolated pharyngeal infection, three (6.0%) had isolated rectal infection, and four (8.0%) had infection detected at more than one anatomical site.

Table 2. Clinical presentation and anatomical site of gonococcal infection (N = 50)

Clinical characteristic	n (%)
Symptom status	
Symptomatic infection	45 (90.0)
Asymptomatic infection	5 (10.0)
Presenting manifestations†	
Urethral/vaginal discharge	34 (68.0)
Dysuria	31 (62.0)
Genital irritation/discomfort	12 (24.0)
Lower abdominal/pelvic discomfort	6 (12.0)
Rectal symptoms	4 (8.0)
Pharyngeal symptoms	3 (6.0)
Primary anatomical pattern	
Urogenital	38 (76.0)
Pharyngeal	5 (10.0)
Rectal	3 (6.0)
Multisite infection	4 (8.0)

All 50 enrolled patients were positive for Neisseria gonorrhoeae by nucleic acid amplification testing and/or culture. NAAT confirmed infection in all participants, while viable N. gonorrhoeae was recovered by culture in 40 patients (80.0%).

Among patients in whom appropriate urethral Gram staining was performed, intracellular Gram-negative diplococci were identified in 29 of 35 specimens (82.9%).

Concomitant Chlamydia trachomatis infection was identified in nine patients (18.0%). Three patients (6.0%) had serological evidence of syphilis requiring evaluation or treatment, while two patients (4.0%) were HIV-positive. Relevant concomitant infections were managed according to institutional STI treatment protocols.

Among the 40 culture-positive isolates, the ceftriaxone MIC ranged from ≤0.016 to 0.25 µg/mL. The MIC50 was 0.032 µg/mL and the MIC90 was 0.125 µg/mL. Most isolates demonstrated low ceftriaxone MIC values; only one isolate had an MIC of 0.25 µg/mL.

Table 3. Laboratory findings and associated sexually transmitted infections

Laboratory parameter	Result
N. gonorrhoeae NAAT positive	50/50 (100.0%)
N. gonorrhoeae culture positive	40/50 (80.0%)
Intracellular Gram-negative diplococci on Gram stain*	29/35 (82.9%)
C. trachomatis coinfection	9/50 (18.0%)
Syphilis seropositivity requiring evaluation/treatment	3/50 (6.0%)
HIV-positive status	2/50 (4.0%)
Ceftriaxone MIC50	0.032 µg/mL
Ceftriaxone MIC90	0.125 µg/mL
Ceftriaxone MIC range	≤0.016–0.25 µg/mL

A rapid clinical response was observed following ceftriaxone treatment. Of the 45 patients who were symptomatic at baseline, 42 (93.3%) experienced complete resolution of symptoms at the first clinical follow-up approximately seven days after treatment. The remaining three patients (6.7%) showed substantial

clinical improvement without clinical deterioration.

Of the 50 treated patients, 48 returned for the predefined microbiological test-of-cure assessment approximately 14 days after treatment. Forty-seven of these 48 patients had negative microbiological results at all previously positive evaluable sites, corresponding to a per-protocol microbiological cure rate of 97.9% (95% CI: 88.9–99.9%).

When the two patients lost to follow-up were conservatively considered treatment non-cures, the modified intention-to-treat microbiological cure rate was 94.0% (47/50; 95% CI: 83.5–98.7%).

One patient remained microbiologically positive at the test-of-cure visit, resulting in a microbiological failure rate of 2.1% among evaluable participants. Review of the patient's history did not identify definite post-treatment sexual re-exposure before the positive test-of-cure result, and the case was therefore classified as a suspected treatment failure rather than definite reinfection.

Table 4. Clinical and microbiological efficacy of ceftriaxone

Outcome	n/N (%)	95% CI
Complete symptom resolution at approximately Day 7*	42/45 (93.3)	81.7–98.6
Clinical improvement without complete resolution at Day 7*	3/45 (6.7)	—
Test-of-cure completed	48/50 (96.0)	—
Microbiological cure, per-protocol population	47/48 (97.9)	88.9–99.9
Microbiological failure	1/48 (2.1)	—
Microbiological cure, modified intention-to-treat analysis†	47/50 (94.0)	83.5–98.7
Definite reinfection before test of cure	0/48 (0)	—

Treatment efficacy remained high across anatomical sites. All 37 evaluable patients with isolated urogenital infection achieved microbiological cure, giving a site-specific patient-level cure proportion of 100%. All patients with isolated rectal infection and all evaluable patients with multisite infection were also microbiologically negative at follow-up.

Among five evaluable patients with isolated pharyngeal gonorrhoea, four achieved microbiological cure, corresponding to an observed cure rate of 80.0%. The single microbiological failure occurred in this group. Because only one failure occurred in the entire study, comparisons between anatomical sites were statistically underpowered. Comparison of pharyngeal with non-pharyngeal infection using Fisher's exact test did not demonstrate a statistically significant difference in cure (P = 0.104).

Table 5. Microbiological cure according to anatomical pattern of infection

Anatomical pattern	Evaluable patients, n	Microbiological cure, n (%)	Failure, n (%)
Urogenital	37	37 (100.0)	0
Pharyngeal	5	4 (80.0)	1 (20.0)
Rectal	3	3 (100.0)	0
Multisite	3	3 (100.0)	0
Overall	48	47 (97.9)	1 (2.1)

Fisher's exact test comparing pharyngeal versus non-pharyngeal infection: P = 0.104.

The wide confidence intervals associated with rectal, pharyngeal, and multisite estimates should be considered when interpreting these findings because of the small number of patients within these subgroups.

Ceftriaxone MIC data were available for 40 culture-positive baseline isolates. Eighteen isolates (45.0%) had MIC values ≤0.016 µg/mL, 11 (27.5%) had an MIC of 0.032 µg/mL, seven (17.5%) had an MIC of 0.064 µg/mL, three (7.5%) had an MIC of 0.125 µg/mL, and one isolate (2.5%) demonstrated an elevated MIC of 0.25 µg/mL.

Of the 38 culture-positive patients who completed the test-of-cure assessment, all 37 patients whose isolates had ceftriaxone MIC values ≤0.125 µg/mL achieved microbiological eradication. The only patient with an isolate demonstrating an MIC of 0.25 µg/mL remained microbiologically positive at follow-up. Because only a single isolate occurred in the highest MIC category, formal modelling of MIC as an independent predictor of treatment failure was considered inappropriate.

Table 6. Distribution of baseline ceftriaxone MIC and microbiological outcome

Ceftriaxone MIC (µg/mL)	Baseline isolates, n (%)	Evaluable at TOC, n	Microbiological cure, n (%)
≤0.016	18 (45.0)	17	17 (100.0)
0.032	11 (27.5)	10	10 (100.0)
0.064	7 (17.5)	7	7 (100.0)
0.125	3 (7.5)	3	3 (100.0)
0.25	1 (2.5)	1	0 (0)
Total	40 (100.0)	38	37 (97.4)

Ceftriaxone was generally well tolerated. Ten patients (20.0%) reported at least one treatment-emergent adverse event. The most frequent event was transient pain at the intramuscular injection site, reported by seven patients (14.0%). Nausea occurred in three patients (6.0%), diarrhoea in two (4.0%), and dizziness and transient rash were each reported by one patient (2.0%). Because individual patients could report more than one adverse event, the sum of event frequencies exceeded the number of affected participants.

All reported adverse events were mild or moderate and resolved spontaneously or with symptomatic treatment. No anaphylaxis, serious drug-related adverse event, hospitalization, treatment discontinuation, or death occurred.

Figure 1. Anatomical distribution of Neisseria gonorrhoeae infection among the study participants, showing predominance of urogenital infection

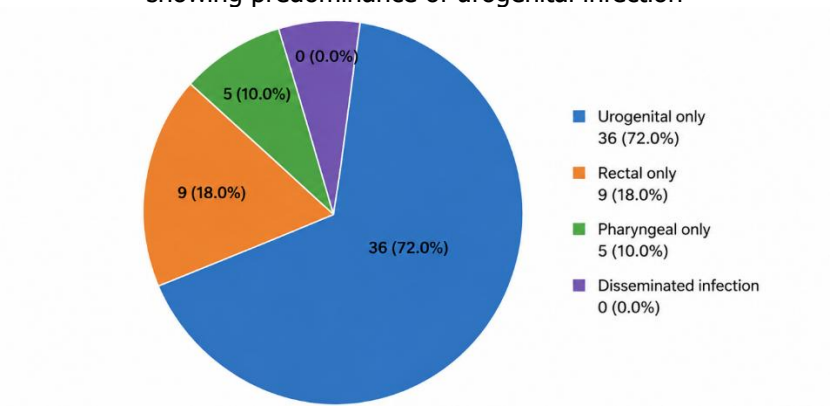

Figure 1 illustrates the anatomical distribution of Neisseria gonorrhoeae infection among the 50 study participants. Urogenital infection was the most common presentation, observed in 38 patients (76.0%), indicating that the genital tract was the predominant site of infection in this cohort. Pharyngeal infection was identified in 5 patients (10.0%), rectal infection in 3 patients (6.0%), and multisite infection in 4 patients (8.0%). Overall, the figure highlights the clear predominance of urogenital gonorrhoea compared with extragenital and multisite involvement.

Figure 2. Site-specific microbiological cure rates following ceftriaxone treatment, demonstrating complete eradication in evaluable urogenital, rectal, and multisite infections and a lower observed cure proportion for pharyngeal infection

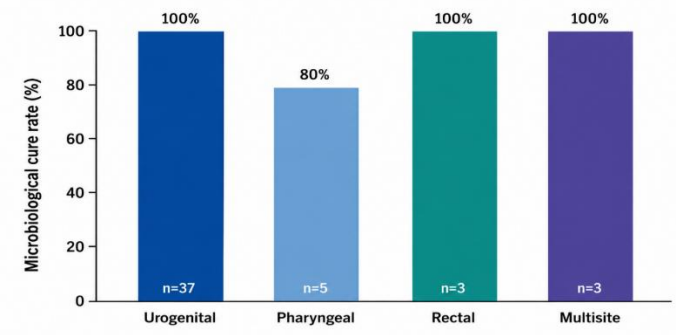

Figure 2 presents the site-specific microbiological cure rates following ceftriaxone treatment among evaluable patients with gonorrhoea. Complete microbiological eradication was achieved in all patients with urogenital infection (37/37, 100.0%), rectal infection (3/3, 100.0%), and multisite infection (3/3, 100.0%). In contrast, the observed cure rate for pharyngeal infection was lower, with microbiological cure achieved in 4 of 5 patients (80.0%). These findings indicate that ceftriaxone was highly effective across most anatomical sites, although pharyngeal gonorrhoea showed a comparatively lower observed response.

DISCUSSION

This study evaluated the clinical and microbiological efficacy of a single dose of intramuscular ceftriaxone 1 g for uncomplicated gonorrhoea and showed a high overall therapeutic response. Among the 48 patients who completed microbiological test-of-cure assessment, 47 achieved microbiological eradication, corresponding to a per-protocol cure rate of 97.9%. Clinical improvement was similarly favourable, with complete resolution of presenting symptoms in 93.3% of symptomatic patients by approximately seven days after treatment. These observations support the continued effectiveness of high-dose ceftriaxone against uncomplicated Neisseria gonorrhoeae infection while simultaneously emphasising the importance of surveillance for emerging reduced susceptibility.

The microbiological cure rate observed in the present study is consistent with contemporary evidence demonstrating excellent activity of ceftriaxone against gonococcal infection. Aoki et al. evaluated ceftriaxone 1 g monotherapy for extragenital gonorrhoea and reported an overall efficacy of 98.1%, with cure rates of 97.8% for pharyngeal and 98.6% for rectal infections [10]. Their results are remarkably close to the overall 97.9% cure observed in the present study and support the capacity of 1-g ceftriaxone monotherapy to achieve reliable microbiological eradication at both genital and extragenital sites. Importantly, Aoki et al. found no significant reduction in efficacy when comparing ceftriaxone monotherapy with combination therapy, supporting antimicrobial stewardship approaches that avoid unnecessary additional antimicrobial exposure when concomitant infections have been excluded [10].

Further evidence supporting the high efficacy of ceftriaxone comes from a recent randomised clinical trial by Bížová et al. [11]. In that study, patients with uncomplicated urogenital, rectal, or pharyngeal gonorrhoea receiving ceftriaxone 1 g plus azithromycin achieved 100% microbiological clearance in the per-protocol population. In contrast, cefixime-based therapy showed lower overall effectiveness, and the treatment failures observed with cefixime occurred exclusively among patients with pharyngeal infection [11]. Although concomitant azithromycin in the ceftriaxone arm prevents direct comparison with ceftriaxone monotherapy in the present study, these findings reinforce the superior reliability of parenteral ceftriaxone, particularly when anatomical sites associated with more difficult eradication are involved.

An important observation in the present study was the difference in the observed response according to anatomical site. All evaluable patients with isolated urogenital and rectal infections achieved microbiological cure, whereas four of five patients with isolated pharyngeal infection were cured. The resulting observed pharyngeal cure rate of 80% should be interpreted cautiously because only five patients were included in this subgroup, and the difference between pharyngeal and non-pharyngeal infection did not reach statistical significance. Nevertheless, the location of the only microbiological failure at the pharyngeal site is clinically meaningful and consistent with the broader literature.

Pharyngeal gonorrhoea has repeatedly emerged as the anatomical reservoir most closely associated with cephalosporin treatment failure. A recent systematic review and meta-analysis by Miari et al. examined minimum inhibitory concentrations among documented extended-spectrum cephalosporin treatment failures. They demonstrated that ceftriaxone failure can occur even when MIC values remain below conventional resistance thresholds [12]. The authors reported a pooled mean ceftriaxone MIC of approximately 0.10 mg/L among treatment-failure isolates and highlighted that pharyngeal failures may occur at comparatively modest MIC values. These findings indicate that in vitro susceptibility alone does not completely predict therapeutic success at the pharyngeal site. Anatomical pharmacokinetic factors likely contribute substantially to treatment outcomes [12].

This interpretation is strengthened by the recent review by Fagan et al., which identified

33 probable or confirmed ceftriaxone treatment failures reported internationally [13]. Only eight met stringent criteria for confirmed treatment failure, but most confirmed cases involved pharyngeal infection. The authors emphasised that reduced antimicrobial penetration, variability in antibiotic exposure within oropharyngeal tissues, difficulties in diagnosing asymptomatic pharyngeal infection, and limitations in surveillance may collectively explain the predominance of pharyngeal failures [13]. Therefore, the single pharyngeal failure observed in the present cohort should not be interpreted as evidence that ceftriaxone is generally ineffective for pharyngeal gonorrhoea; rather, it reinforces the importance of site-specific follow-up and careful investigation of persistent pharyngeal positivity.

The antimicrobial susceptibility findings also merit particular consideration. Most baseline isolates demonstrated low ceftriaxone MIC values, with an MIC50 of 0.032 µg/mL and an MIC90 of 0.125 µg/mL. Of the 40 cultured isolates, only one demonstrated a ceftriaxone MIC of 0.25 µg/mL. Notably, this isolate was also associated with persistent microbiological positivity at the test-of-cure assessment. Although a single observation cannot establish a statistically valid MIC-outcome relationship, the concordance between the highest MIC and the only treatment failure is biologically plausible and warrants attention.

Recent Indian surveillance data provide an important context for this finding. Sood et al. analysed approximately 15 years of gonococcal antimicrobial susceptibility data from North India. They found high resistance to older agents such as penicillin, tetracycline, and ciprofloxacin, whereas susceptibility to ceftriaxone and cefixime remained above 90% [14]. Importantly, the study identified no ceftriaxone-resistant isolates during the study period, and observed no significant ceftriaxone MIC creep. Nevertheless, the authors specifically emphasised the importance of continued MIC-based monitoring because subtle increases in cephalosporin MIC values could precede clinically important resistance [14]. The predominance of low ceftriaxone MICs in the current study therefore agrees broadly with contemporary Indian experience. At the same time, the single isolate with an MIC of 0.25 µg/mL emphasises why ongoing phenotypic surveillance should accompany clinical efficacy studies.

Similar concerns have been reported in multicentric Indian surveillance. Kulkarni et al. evaluated 124 N. gonorrhoeae isolates collected from five Indian cities and found extensive resistance to ciprofloxacin, penicillin, and tetracycline. Most isolates remained susceptible to ceftriaxone and cefixime, although two strains demonstrated decreased susceptibility to these extended-spectrum cephalosporins [15]. Taken together with the present observations, these findings suggest that ceftriaxone continues to retain strong activity in India, but this efficacy cannot be assumed to remain stable indefinitely. Routine culture, MIC determination in selected cases, and referral of isolates associated with suspected treatment failure are therefore integral components of antimicrobial stewardship.

It is also important that the isolate with an MIC of 0.25 µg/mL in the present study is described as having an elevated ceftriaxone MIC or reduced susceptibility signal, rather than being automatically classified as ceftriaxone-resistant. Contemporary Gonococcal Isolate Surveillance Project criteria use ceftriaxone MIC ≥0.125 µg/mL as an epidemiological indicator of an elevated MIC. In contrast, formal ceftriaxone resistance criteria for N. gonorrhoeae remain incompletely defined in current CLSI-based surveillance frameworks [20]. This distinction matters for accurate interpretation and prevents overstating antimicrobial resistance based on a single MIC measurement.

Another clinically relevant observation was the detection of Chlamydia trachomatis coinfection in 18% of participants. Coinfection has important therapeutic implications because successful eradication of gonorrhoea does not adequately treat concomitant chlamydial disease. Indian evidence indicates considerable variation in gonorrhoea-chlamydia coinfection rates. Aravinda et al., in a prospective study of symptomatic STI clinic attendees in New Delhi, detected N. gonorrhoeae–C. trachomatis coinfection in approximately 5% of their study population [16]. Conversely, Templeton et al. reported chlamydial coinfection in 16.4% of patients with anogenital gonorrhoea, a figure close to the 18% observed in the present cohort [17]. Variability across studies may reflect differences in patient populations, sexual networks, anatomical sampling, diagnostic methods, and regional epidemiology. Nevertheless, these findings support routine testing for C. trachomatis when gonorrhoea is diagnosed, rather than relying exclusively on empirical combination therapy.

The high proportion of symptomatic patients in the present study may partly reflect the clinical

setting and sex distribution of the cohort. Approximately 82% of participants were male, and urethral or genital discharge and dysuria were the predominant presenting complaints. Symptomatic urethral gonorrhoea in men is more likely to lead to prompt healthcare attendance and microbiological diagnosis than asymptomatic cervical, pharyngeal, or rectal infection. Consequently, the study population may underrepresent asymptomatic and extragenital gonorrhoea. This consideration is particularly important when extrapolating the results to broader populations where screening rather than symptoms drives case detection.

The use of a standardised microbiological test of cure was a methodological strength because clinical symptom resolution alone cannot reliably demonstrate eradication. In this cohort, clinical cure was high, but microbiological testing identified one persistent infection despite substantial overall clinical improvement. This distinction is particularly relevant for pharyngeal gonorrhoea, where infection may persist without symptoms. However, interpretation of positive post-treatment NAAT requires caution. Bissessor et al. demonstrated persistence of gonococcal DNA in a proportion of patients at both seven and 14 days after therapy. They showed that persistent NAAT positivity may be related to elevated antimicrobial MICs, residual nucleic acid, or reinfection [19]. In the current study, obtaining culture whenever feasible in patients with a positive test of cure is therefore essential to distinguish viable persistent infection from residual nucleic acid detection.

The safety findings were also favourable. Only 20% of patients reported any treatment-emergent adverse event, and the majority were mild. Injection-site pain was the most frequent adverse event, occurring in 14% of participants, followed by nausea and diarrhoea. No serious adverse event, anaphylaxis, treatment discontinuation, hospitalisation, or death was recorded. These findings are consistent with the established safety profile of single-dose ceftriaxone. Dresser and Wilby, in a systematic review and meta-analysis assessing ceftriaxone, cefixime, and gentamicin for gonorrhoea, found no major safety signal associated with ceftriaxone and identified injection-site pain as one of the more frequently reported adverse effects of intramuscular treatment [18]. Thus, the high efficacy observed in the current study was achieved without a clinically important compromise in tolerability.

The present study has several strengths. Microbiological confirmation was required for study inclusion, treatment was standardised using ceftriaxone 1 g intramuscularly, and clinical as well as microbiological outcomes were assessed. The study examined anatomical site-specific efficacy, incorporated culture where feasible, and included ceftriaxone MIC values for most viable isolates. Furthermore, a test-of-cure approach allowed identification of persistent infection that might otherwise have remained undetected.

Several limitations must nevertheless be acknowledged. First, the sample size was relatively small, particularly for rectal and pharyngeal infections, resulting in wide uncertainty around site-specific cure estimates. The 80% observed pharyngeal cure proportion, for example, was based on only five evaluable patients and should not be interpreted as a precise estimate of ceftriaxone efficacy. Second, this single-centre study had a relatively short recruitment period (May to July 2026), potentially limiting generalizability to other geographic regions and patient populations. Third, 82% of participants were male, limiting assessment of treatment outcomes among women. Fourth, viable culture isolates were obtained from 80% rather than all patients, restricting universal MIC analysis. Fifth, two participants did not complete microbiological follow-up. Although this attrition was limited, the modified intention-to-treat cure estimate fell from 97.9% to 94.0% when missing outcomes were conservatively considered treatment failures. Finally, the protocol did not incorporate molecular typing. Whole-genome sequencing or another validated molecular typing method would better distinguish genuine treatment failure from reinfection in cases of persistent positivity.

Despite these limitations, the findings have important clinical and public health implications. The high microbiological cure rate confirms that ceftriaxone remains a highly effective therapeutic option for uncomplicated gonorrhoea, including urogenital and rectal infection. At the same time, the occurrence of a persistent pharyngeal infection associated with the highest baseline ceftriaxone MIC highlights the potential vulnerability of pharyngeal gonorrhoea to therapeutic failure. Increasing dependence on ceftriaxone as the principal reliable empirical therapy makes preservation of its effectiveness essential. Culture-based antimicrobial susceptibility testing, careful investigation of suspected

treatment failures, appropriate testing for concomitant infections, partner management, avoidance of unnecessary antimicrobial exposure, and continued regional surveillance should therefore remain central components of gonorrhoea management.

CONCLUSION

Single-dose intramuscular ceftriaxone 1 g demonstrated excellent overall clinical and microbiological efficacy and favourable tolerability in the present cohort. Complete microbiological eradication was achieved in all evaluable urogenital and rectal infections. In contrast, the only microbiological failure occurred at the pharyngeal site in a patient whose baseline isolate demonstrated the highest ceftriaxone MIC. These findings support the continued therapeutic role of ceftriaxone while emphasising that high population-level efficacy should not lead to complacency. Larger multicentre studies incorporating systematic extragenital sampling, culture, standardised MIC testing, molecular characterisation of isolates, and extended follow-up are required to identify early changes in cephalosporin susceptibility and preserve effective treatment options for gonorrhoea.

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