

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Gonococcal and Non-Gonococcal Urethritis in a Global Travel Hub: A Retrospective Analysis of Syndromic Management, Suboptimal Cefixime Monotherapy, and the Public Health Crisis of Patient Retention in Bali, Indonesia

Andrew Wicaksono¹, I Gusti Ayu Agung Elis Indira^{1*}, Ni Made Dwi Puspawati¹, Aditya Permana¹, Nyoman Suryawati¹

¹Department of Dermatology and Venereology, Faculty of Medicine, Universitas Udayana/Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Indonesia

ARTICLE INFO

Keywords:

Antimicrobial resistance
Cefixime
Gonorrhoea
Neisseria gonorrhoeae
Urethritis

*Corresponding author:

I Gusti Ayu Agung Elis Indira

E-mail address:

elisindira@unud.ac.id

All authors have reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/bsm.v9i11.1447>

ABSTRACT

Background: The inexorable rise of antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* represents a formidable threat to global public health, jeopardizing the efficacy of last-line treatments for gonococcal urethritis (GO). Southeast Asia is a recognized epicenter for the emergence and dissemination of AMR, yet granular surveillance data from many high-risk localities remain critically sparse. This study aimed to provide a comprehensive characterization of the clinical epidemiology, frontline management practices, and patient outcomes of male urethritis at a tertiary referral center in Bali, Indonesia—a major international crossroads for tourism and migration. **Methods:** A retrospective, cross-sectional analysis was conducted on the medical records of male patients diagnosed with urethritis at the Dermatology and Venereology Polyclinic of Ngoerah Hospital between January 1st, 2021, and December 31st, 2024. A rigorous screening process of 215 initial records was undertaken to identify eligible cases. Data on sociodemographics, behavioral risk factors, clinical presentation, syndromic diagnosis, prescribed pharmacotherapy, and follow-up adherence were systematically extracted and analyzed using descriptive and comparative statistics. **Results:** From the initial cohort, 58 male patients met the final inclusion criteria. The cohort was predominantly diagnosed with GO (n=39, 67.2%) over non-gonococcal urethritis (NGO) (n=19, 32.8%). Patients were primarily of productive age (25–44 years, 58.6%) and reported high-risk behaviors, including multiple sexual partners (65.5%). A critical deviation from international treatment guidelines was identified: 97.4% (38/39) of GO patients received oral cefixime 400 mg monotherapy, a regimen no longer recommended for first-line use due to AMR concerns. Furthermore, a profound fracture in the care cascade was evident, with an overall loss-to-follow-up rate of 58.6% (34/58). This failure was most pronounced in the GO cohort, where 76.9% (30/39) of patients did not return for scheduled follow-up, a rate significantly higher than the 21.1% (4/19) observed in the NGO cohort (p<0.001). **Conclusion:** The clinical management of gonorrhoea at this major Indonesian referral center is defined by two systemic failures: the routine prescription of a suboptimal antimicrobial monotherapy and a near-total collapse of patient follow-up. This combination, situated in a high-transience international hub, creates an unmonitored, high-risk environment for the selection, amplification, and global dissemination of antimicrobial-resistant *N. gonorrhoeae*. These findings signal an urgent imperative to align local therapeutic protocols with evidence-based global standards and to implement robust, innovative strategies to ensure patient retention and verify the cure.

1. Introduction

Sexually transmitted infections (STIs) constitute a persistent and escalating challenge to global public health, exacting a significant toll on individual health,

healthcare systems, and socioeconomic development.¹

The World Health Organization (WHO) estimates that over one million curable STIs are acquired daily worldwide, a testament to their pervasive and endemic

nature.² Among bacterial STIs, gonorrhoea, caused by the obligate human pathogen *Neisseria gonorrhoeae*, remains a primary cause of morbidity. In 2020 alone, an estimated 82.4 million new cases occurred in adults globally, manifesting in syndromes such as urethritis, cervicitis, proctitis, and pharyngitis. If inadequately treated, these infections can lead to devastating long-term sequelae, including pelvic inflammatory disease, ectopic pregnancy, chronic pelvic pain, and infertility. Furthermore, the mucosal inflammation caused by gonococcal infection significantly enhances the biological susceptibility to and transmission of the human immunodeficiency virus (HIV).³

The effective control of gonorrhoea is profoundly threatened by the remarkable and relentless ability of *N. gonorrhoeae* to develop antimicrobial resistance (AMR).⁴ This bacterium has systematically developed resistance to every class of antibiotic ever used for its treatment, from the sulfonamides of the 1930s to penicillins, tetracyclines, and, more recently, fluoroquinolones and macrolides.⁵ This evolutionary trajectory has progressively narrowed our therapeutic options, forcing a reliance on the extended-spectrum cephalosporins (ESCs) as the last remaining highly effective class for empirical, single-dose therapy.

The emergence of strains with reduced susceptibility and outright resistance to ESCs, particularly the oral agent cefixime and the injectable agent ceftriaxone, represents a critical inflection point. This has culminated in the identification of extensively drug-resistant (XDR) and pandrug-resistant strains, fueling the specter of untreatable gonorrhoea. In recognition of this grave threat, the WHO has designated drug-resistant *N. gonorrhoeae* as a "priority pathogen," demanding urgent investment in research, development of new therapeutics, and enhanced global surveillance.

Central to the fight against AMR is a robust understanding of pharmacokinetic and pharmacodynamic (PK/PD) principles.⁶ Injectable ceftriaxone is now the universally recommended first-line agent because it achieves high, sustained

bactericidal concentrations in the blood and at mucosal sites of infection (urethra, cervix, pharynx) that far exceed the minimum inhibitory concentrations (MICs) for most circulating strains. In contrast, oral cefixime achieves lower peak serum concentrations and has a shorter half-life, creating a PK/PD profile that is less reliable for eradicating infections, particularly in the pharynx, which often serves as an asymptomatic reservoir for transmission and a niche for the selection of resistance. The continued use of cefixime, especially as monotherapy, exerts significant selective pressure, favoring the survival and propagation of strains with mutations conferring reduced cephalosporin susceptibility.⁷

Global surveillance, primarily coordinated through the WHO's Gonococcal Antimicrobial Surveillance Programme (GASP), is fundamental to monitoring AMR trends and informing evidence-based treatment guidelines.⁸ However, significant geographical gaps in high-quality surveillance persist. Southeast Asia has been repeatedly identified as a critical "crucible" for the emergence and international spread of resistant gonococcal strains, driven by a confluence of factors including high population density, unregulated access to antimicrobials, and complex sexual networks.⁹ Yet, robust, contemporary AMR and clinical practice data from many parts of this epidemiologically vital region are alarmingly scarce. This information vacuum severely hampers the ability of local and global health authorities to detect and respond to emerging resistance threats before they achieve widespread dissemination.

Within this context, Bali, Indonesia, represents a unique and highly significant setting for investigation. As one of the world's premier international tourist destinations, Bali functions as an epidemiological crossroads where local, national, and international sexual networks converge. The high degree of population transience, involving tourists, expatriates, and migrant workers, creates a dynamic environment that can facilitate the rapid introduction and dissemination of diverse STI pathogens and their resistance determinants across vast geographical

distances. The frontline clinical management practices in such a setting are, therefore, not merely of local concern but of global public health significance. Despite this, local data on the real-world management of urethritis and patient outcomes in Bali are limited.¹⁰

This study aims to address this critical knowledge gap through a comprehensive retrospective analysis of male urethritis cases at a major tertiary referral hospital in Bali. The novelty and importance of this research lie in its critical evaluation of frontline clinical practices in an under-surveilled, high-risk region. By providing a granular snapshot of syndromic management protocols, prescribed therapies, and, crucially, patient follow-up rates, this study seeks to identify potential misalignments between local practice and international, evidence-based guidelines. The primary objectives were to describe the sociodemographic and behavioral characteristics of male patients presenting with urethritis, to determine the relative prevalence of syndromically diagnosed gonococcal versus non-gonococcal urethritis, to document the antimicrobial regimens prescribed for each diagnosis, and to quantify patient adherence to scheduled follow-up appointments and identify disparities between diagnostic groups.

2. Methods

A retrospective, descriptive, cross-sectional study was conducted by reviewing the medical records at the Dermatology and Venereology Polyclinic of Ngoerah General Hospital in Denpasar, Bali, Indonesia. This public hospital serves as the main provincial tertiary referral center for Bali, providing specialized diagnostic and therapeutic services for a wide spectrum of dermatological and venereological conditions for both the resident population and visitors. The study protocol was designed and executed in accordance with the ethical principles outlined in the Declaration of Helsinki and received full ethical clearance from the Institutional Review

Board of the Faculty of Medicine, Universitas Udayana, and Prof. Dr. I.G.N.G. Ngoerah General Hospital.

The study population included all new male patients who presented to the polyclinic and received a final diagnosis of urethritis between January 1st, 2021, and December 31st, 2024. A multi-stage screening process was employed to identify the final study cohort. First, the hospital's electronic medical record (EMR) and paper-based archives were searched for male patients presenting within the study period with relevant chief complaints or diagnoses, including "urethritis," "urethral discharge," and "dysuria." This initial search yielded 215 unique patient records. These records were then manually screened for eligibility by two independent researchers. Inclusion criteria were: (1) male gender; (2) age ≥ 15 years; (3) a definitive clinical diagnosis of either gonococcal urethritis (GO) or non-gonococcal urethritis (NGO) recorded by a specialist dermatologist-venereologist; and (4) sufficient data on key variables, including diagnosis, prescribed treatment, and demographic information. Exclusion criteria were: (1) female gender (n=48); (2) final diagnosis other than urethritis, such as balanitis, urinary tract infection, or prostatitis (n=71); and (3) critically incomplete or ambiguous medical records where either the definitive diagnosis or the prescribed antimicrobial therapy could not be unequivocally determined (n=38). This rigorous screening process resulted in a final sample of 58 eligible patient records for inclusion in the analysis (Figure 1).

A standardized data extraction form was developed and pre-tested to ensure consistency. Data were systematically collected from the selected medical records and entered into a secure, de-identified database to protect patient confidentiality. The following variables were extracted: final diagnosis: The definitive diagnosis of GO or NGO. In this clinical setting, a syndromic approach is standard.

Flow Diagram of Patient Record Selection

A visual representation of the screening and selection process for the study cohort.

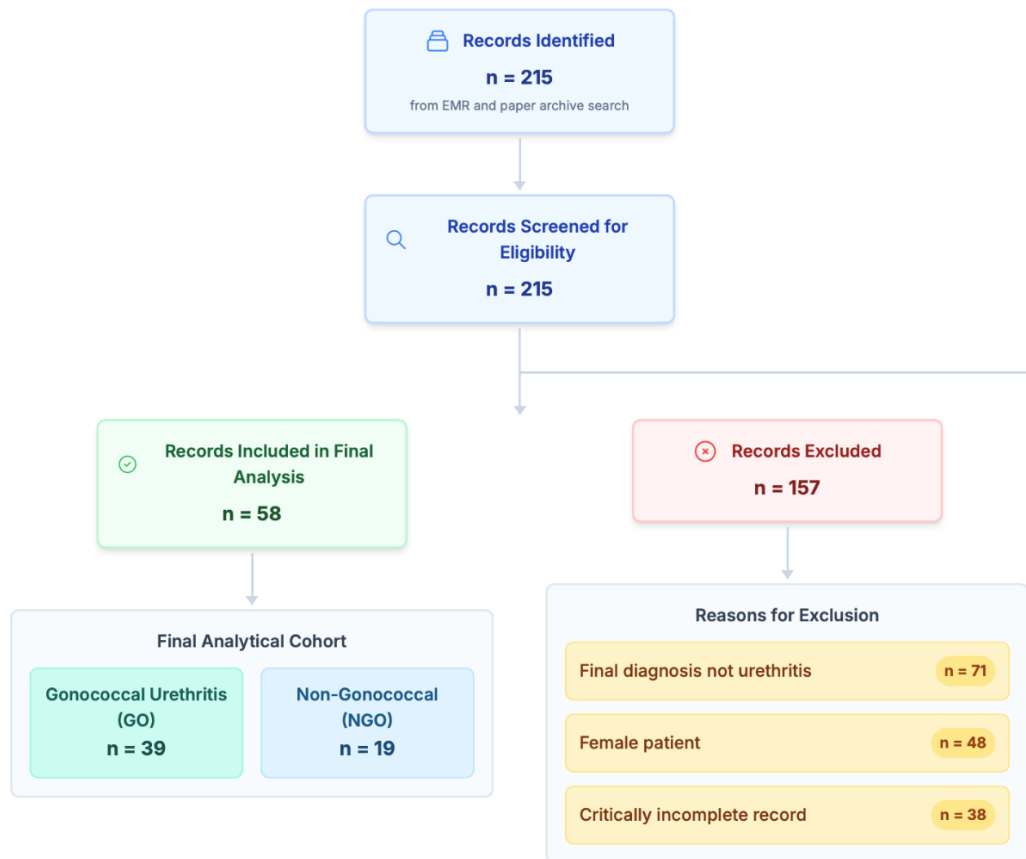


Figure 1. Flow diagram of patient record selection.

A diagnosis of GO was established based on the presence of typical clinical signs (purulent or mucopurulent urethral discharge) combined with microscopic confirmation of gram-negative intracellular diplococci (GNID) on a Gram-stained urethral smear. A diagnosis of NGO was made in patients presenting with clinical urethritis (mucoid/clear discharge, dysuria) and microscopic evidence of urethral inflammation (defined as ≥ 5 polymorphonuclear leukocytes [PMNs] per high-power field [HPF] on a urethral smear) in the absence of GNID; Sociodemographic Data: Age (categorized as 15–24, 25–44, and 45–64 years), highest level of education attained, and occupation; Behavioral and clinical risk factors: Documented history of prior STIs,

HIV status (as recorded in the patient file), number of sexual partners in the preceding six months (categorized as single vs. multiple), type of sexual partner (girlfriend, wife, commercial sex worker, foreigner), and self-reported sexual orientation (heterosexual, homosexual/men who have sex with men [MSM], bisexual); Clinical Presentation: Predominant character of urethral discharge as documented by the clinician (purulent, mucopurulent, or mucoid/clear) and the documented presence or absence of dysuria; Pharmacotherapy: The specific antimicrobial agent(s), dosage, and duration prescribed at the initial consultation; and Follow-up Status: Patient adherence to a scheduled follow-up appointment, which was typically recommended for 7–

14 days post-treatment. Adherence was defined as a documented return visit to the clinic within this specified period. Non-adherence was defined as the absence of a documented return visit and classified as "lost to follow-up." All collected data were coded and analyzed using IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp). Descriptive statistics were employed to summarize the characteristics of the cohort. Categorical variables were presented as frequencies (n) and percentages (%). To investigate associations between categorical variables, comparative analyses were performed. The Chi-square (χ^2) test was used for comparisons between the GO and NGO groups. For analyses involving cells with an expected count of less than 5, Fisher's exact test was used to ensure statistical validity. A two-tailed p-value of <0.05 was considered the threshold

for statistical significance.

3. Results

The systematic screening of medical records is detailed in Figure 1. Of the 215 records initially identified, 157 were excluded, primarily due to being for female patients, having a final diagnosis other than urethritis, or containing critically incomplete data. The final analytical cohort comprised 58 male patients who fully met the inclusion criteria. Of the 58 patients included, 39 (67.2%) were diagnosed with gonococcal urethritis (GO), and 19 (32.8%) were diagnosed with non-gonococcal urethritis (NGO), underscoring the significant local burden of gonorrhoea. The detailed sociodemographic and behavioral characteristics of the patient cohort, stratified by diagnosis, are presented in Table 1.

Table 1. Comparative analysis of patient characteristics.

Sociodemographic, Behavioral, and Clinical Data of Male Patients with Urethritis in Bali, Indonesia (2021–2024)

VARIABLE	CATEGORY	TOTAL (N=58)	URETHRITIS GO (N=39)	URETHRITIS NGO (N=19)	P-VALUE
 Age Group (years)	15–24	20 (34.5%)	15 (38.5%)	5 (26.3%)	0.461
	25–44	34 (58.6%)	21 (53.8%)	13 (68.4%)	
	45–64	4 (6.9%)	3 (7.7%)	1 (5.3%)	
 Education	Junior High	11 (19.0%)	5 (12.8%)	6 (31.6%)	0.048*
	Senior High	35 (60.3%)	28 (71.8%)	7 (36.8%)	
	College	12 (20.7%)	6 (15.4%)	6 (31.6%)	
 Occupation	Student	9 (15.5%)	9 (23.1%)	0 (0.0%)	<0.001*
	Tourism Related	13 (22.4%)	5 (12.8%)	8 (42.1%)	
	Other (Private, Laborer)	36 (62.1%)	25 (64.1%)	11 (57.9%)	
 Number of Partners	Single	20 (34.5%)	13 (33.3%)	7 (36.8%)	0.803
	Multiple	38 (65.5%)	26 (66.7%)	12 (63.2%)	
 Sexual Orientation	Heterosexual	35 (60.3%)	23 (59.0%)	12 (63.2%)	0.531
	Homosexual (MSM)	17 (29.3%)	13 (33.3%)	4 (21.1%)	
	Bisexual	6 (10.3%)	3 (7.7%)	3 (15.8%)	
HIV Status	Positive	3 (5.2%)	3 (7.7%)	0 (0.0%)	0.289
Prior STI History	Yes	14 (24.1%)	8 (20.5%)	6 (31.6%)	0.368

Note: Percentages may not sum to 100 due to rounding. * Statistically significant difference (p < 0.05). GO = Gonococcal Urethritis; NGO = Non-Gonococcal Urethritis; MSM = Men who have sex with men.

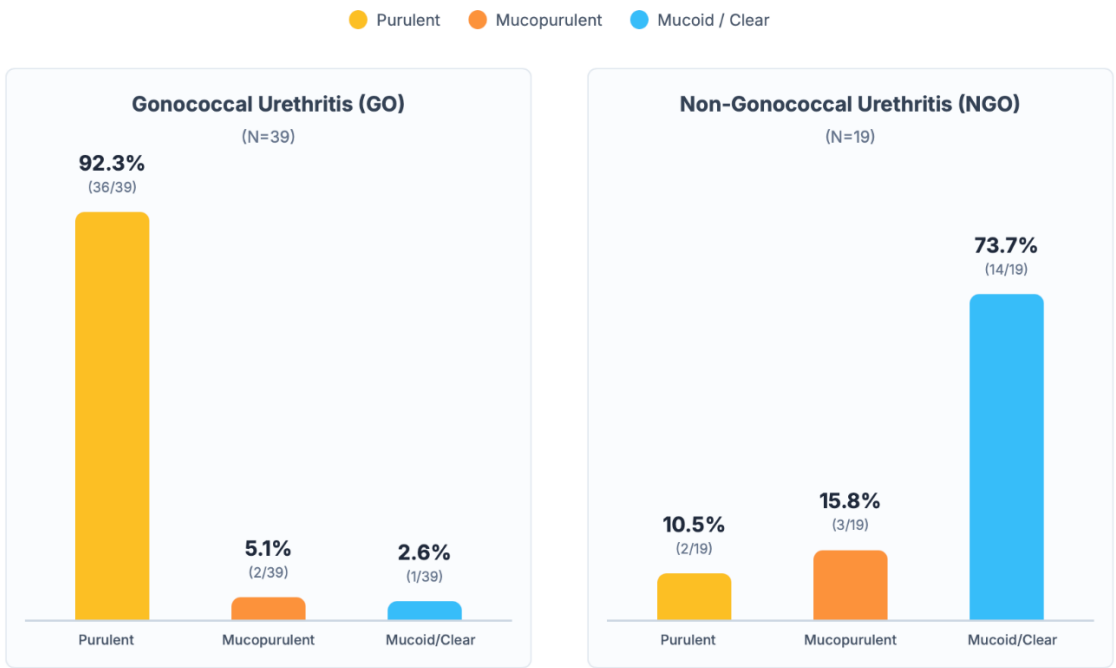
The cohort was predominantly young and middle-aged, with the majority of patients in the 25–44 year age group (n=34, 58.6%), followed by the 15–24 year group (n=20, 34.5%). Most participants had completed senior secondary education (n=35, 60.3%). A statistically significant difference in education level was observed between the groups (p=0.048), with a higher proportion of GO patients having completed senior high school compared to NGO patients. High-risk sexual behavior was common, with nearly two-thirds of the cohort (n=38, 65.5%) reporting multiple sexual partners in the preceding six months. The most frequently reported partner type was a girlfriend (46.6%), followed by commercial sex workers (25.9%). While heterosexuality was the predominant sexual orientation (60.3%), a substantial proportion identified as homosexual (MSM) (29.3%). Three patients (5.2%), all in the GO group, were known to be HIV-positive. Occupation showed a significant association with diagnosis (p<0.001). Notably, all 9

students in the cohort were diagnosed with GO, whereas tourism-related occupations (tourists/guides) were significantly more common in the NGO group (8/13 in this category had NGO).

The clinical presentation at diagnosis differed markedly between the two groups, as illustrated in Figure 2. A purulent urethral discharge was the pathognomonic finding in the GO cohort, reported in 92.3% (36/39) of patients. Conversely, this presentation was rare in the NGO group, occurring in only 10.5% (2/19) of patients. This difference was highly statistically significant (p<0.001). In contrast, a mucoid or clear discharge was the characteristic finding in 73.7% (14/19) of NGO cases but was observed in only one GO patient (2.6%) (p<0.001). Dysuria was a highly prevalent symptom in both cohorts, affecting 84.6% of GO patients and 78.9% of NGO patients, with no significant difference between the groups (p=0.582).

Distribution of Urethral Discharge Characteristics

A comparative visualization of clinical presentation by etiological diagnosis (GO vs. NGO).





Note: The difference in discharge characteristics between GO and NGO groups was highly statistically significant (p < 0.001).

Figure 2. Distribution of urethral discharge characteristics by etiological diagnosis.

The analysis of prescribed antimicrobial therapies revealed a stark and concerning pattern, detailed in Table 2. The management of GO was characterized by near-uniform use of oral cefixime 400 mg as a single dose, which was administered to 97.4% (38/39) of patients in this group. Critically, in all 38 of these cases, cefixime was prescribed as monotherapy, without a concurrent agent (such as azithromycin or doxycycline) recommended by many guidelines to cover potential co-infection with *Chlamydia trachomatis*. Only a single GO patient received a different regimen. For NGO, the treatment was more varied but generally aligned with standard recommendations. The most common regimen was a single 1-gram oral dose of azithromycin (57.9%,

11/19), followed by doxycycline 100 mg twice daily for seven days (31.6%, 6/19). Patient adherence to scheduled follow-up was catastrophically low, representing a major failure in the continuum of care. The overall loss-to-follow-up rate for the entire cohort was 58.6% (34/58). This problem was overwhelmingly concentrated in the GO cohort. Only 23.1% (9/39) of GO patients returned for their scheduled follow-up visit, meaning 76.9% (30/39) were lost. In stark contrast, follow-up adherence in the NGO cohort was high, with 78.9% (15/19) of patients returning as scheduled. This profound difference in follow-up adherence between the two groups was highly statistically significant ($p<0.001$).

Table 2. Prescribed antimicrobial therapy and follow-up adherence.
An analysis of treatment regimens and patient retention by etiological diagnosis.

VARIABLE	URETHRITIS GO (N=39)	URETHRITIS NGO (N=19)	P-VALUE
<div> Prescribed Therapy</div>			
Cefixime 400 mg	38 (97.4%)	2 (10.5%)	<0.001*
Azithromycin 1 g	1 (2.6%)	11 (57.9%)	
Doxycycline 100 mg BID x 7d	0 (0.0%)	6 (31.6%)	
<div> Follow-Up Status</div>			
Adherent (Returned)	9 (23.1%)	15 (78.9%)	<0.001*
Non-Adherent (Lost)	30 (76.9%)	4 (21.1%)	

Note: * Statistically significant difference ($p < 0.05$). Highlighted cells indicate key findings:  suboptimal therapy,  critical loss-to-follow-up, and  high adherence.

4. Discussion

This retrospective study, despite its limitations, provides a critical and unsettling snapshot of the clinical management of male urethritis at a major referral hospital in the global tourism hub of Bali,

Indonesia. The findings expose a confluence of three interconnected issues that carry significant public health ramifications: (1) a high local burden of syndromically diagnosed gonorrhoea, (2) a deeply entrenched clinical practice of treating gonorrhoea

with a suboptimal monotherapy that deviates from current international best practices, and (3) a profound and systemic failure in the continuum of patient care, manifested as a catastrophic rate of loss-to-follow-up.¹¹

The most alarming finding of this study is the near-universal reliance on oral cefixime 400 mg monotherapy for the treatment of gonococcal urethritis. This practice is in direct contravention of current evidence-based guidelines from leading international public health bodies, including the WHO and the U.S. Centers for Disease Control and Prevention (CDC).¹² Both organizations no longer recommend oral cefixime as a first-line agent due to accumulating evidence of rising cefixime MICs globally and its inferior pharmacokinetic profile compared to injectable ceftriaxone. The current standard of care recommended by the CDC is a single 500 mg intramuscular dose of ceftriaxone (1 g for patients weighing ≥ 150 kg), while the WHO recommends a 1 g dose to ensure sufficiently high bactericidal concentrations, particularly for eradicating pharyngeal infections, which are common and often asymptomatic.¹³

The continued reliance on this outdated and suboptimal monotherapy in a high-transmission region like Southeast Asia—a known crucible for gonococcal AMR—poses a grave and unmonitored threat. It creates an ideal ecological niche for the selection of gonococcal strains with mutations that confer reduced cephalosporin susceptibility, effectively paving the way for the emergence of clinical ceftriaxone resistance. Each patient treated with a less effective agent represents a potential instance of treatment failure and a missed opportunity to halt transmission, thereby contributing to the erosion of our last highly effective antibiotic class for gonorrhoea.

The stark deviation from global guidelines observed in this study is unlikely to be the result of arbitrary clinical decisions.¹⁴ Rather, it likely reflects a complex interplay of systemic, logistical, and patient-level factors. While this study cannot definitively determine the root causes, we can speculate on several plausible

drivers: Guideline Lag and Dissemination: There may be a significant lag between the updating of international guidelines by bodies like the WHO and CDC and their adoption and dissemination into national or local institutional protocols in Indonesia. The resources required for continuous medical education and protocol updates can be substantial, leading to inertia in clinical practice; Pharmacoeconomics and Logistics: Cefixime offers significant practical advantages over ceftriaxone. As an oral tablet, it is inexpensive, easy to store, and simple to dispense. In contrast, ceftriaxone is an intramuscular injection that requires reconstitution, sterile supplies like needles and syringes, and a trained healthcare professional to administer it safely.¹⁵ In a busy public polyclinic, the logistical simplicity and lower cost of cefixime may strongly favor its use, especially if institutional budgets are constrained; Patient-Centric Factors: Patients often express a strong preference for oral medications over painful injections. A clinician, aiming to ensure treatment acceptance and initial adherence, may opt for cefixime in the belief that an accepted oral therapy is better than a refused injectable one. This patient-centered consideration, while well-intentioned, can inadvertently contribute to a broader public health risk; Perceived versus Actual Risk: Clinicians may be operating under the assumption that cefixime remains "good enough" for uncomplicated urogenital gonorrhoea, particularly if they are not seeing overt clinical failures in their practice. This perception may not account for the subclinical persistence of infection, especially in the pharynx, or the broader epidemiological risk of selecting for resistance. Understanding these underlying drivers is crucial for designing effective interventions, which must go beyond simple guideline dissemination to address the structural and economic barriers to best-practice implementation.¹⁶

This risk of AMR amplification is profoundly compounded by the second major finding: a catastrophic failure in patient follow-up.¹⁷ An overall loss-to-follow-up rate of 58.6% is deeply concerning,

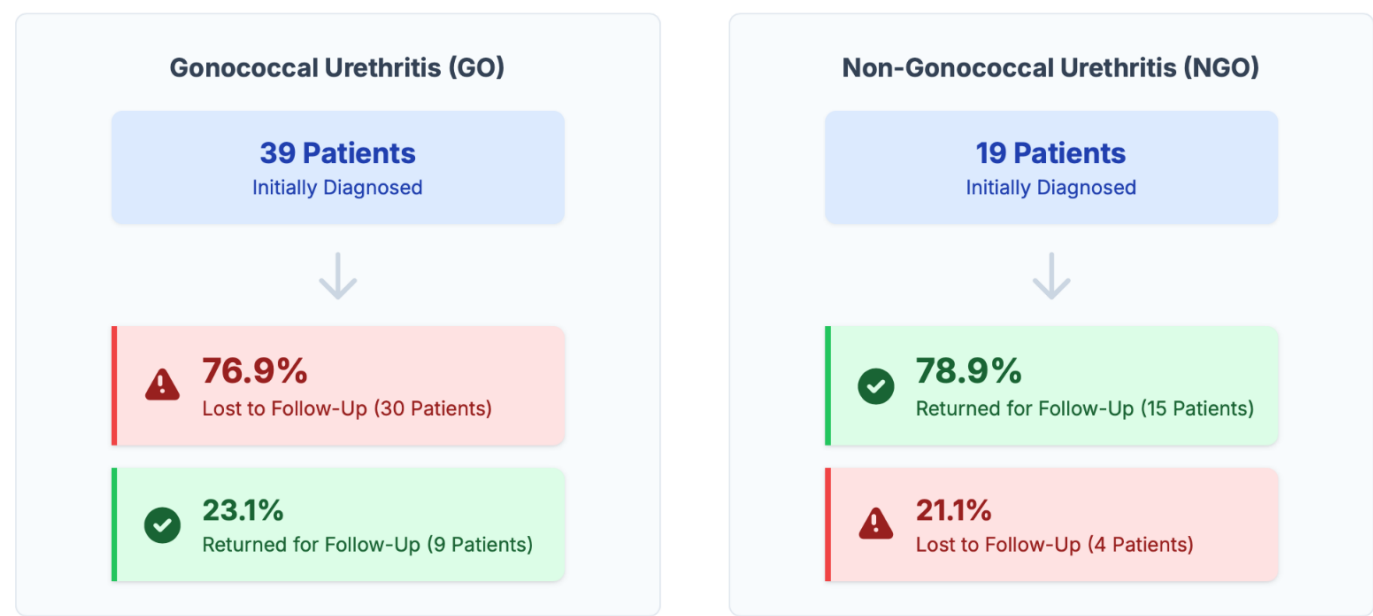
but the 76.9% rate among GO patients represents a complete breakdown in the STI care cascade. The goals of STI management extend far beyond initial symptomatic relief; they encompass verifying microbiological cure (test-of-cure), identifying and managing treatment failures, preventing long-term sequelae, and ensuring partner notification and treatment to break chains of onward transmission. When nearly four out of five patients with a highly infectious disease like gonorrhoea are not seen again, treatment "success" is merely an unsubstantiated assumption (Figure 3).

The stark difference in follow-up adherence between GO (23.1%) and NGO (78.9%) patients is telling and likely reflects the distinct pathophysiology of the infections. Gonorrhoea typically incites an acute, vigorous inflammatory response, leading to the

dramatic and highly distressing purulent discharge observed in our cohort. Effective antibiotic therapy leads to a rapid and marked resolution of these symptoms, often within 24-48 hours. Patients may incorrectly perceive this symptomatic relief as a definitive cure, thus disincentivizing them from returning for a follow-up visit that requires additional time, travel, and potential cost. In contrast, NGO pathogens like *Chlamydia trachomatis* often cause a more indolent, subacute inflammation with milder symptoms that may resolve more slowly, potentially motivating patients to return to confirm the infection has cleared. Social stigma, which may be more pronounced for a "classic" and highly recognizable STI like gonorrhoea, may further discourage patients from re-engaging with the healthcare system.¹⁸

A Fractured Care Cascade

Visualizing the Crisis of Patient Retention in Gonococcal vs. Non-Gonococcal Urethritis



Conclusion: The difference in follow-up adherence between the GO and NGO cohorts is highly statistically significant ($p < 0.001$), revealing a critical failure in the care cascade specifically for patients with gonococcal infections.

Figure 3. A fractured care cascade: The crisis of patient retention.

The study's setting in a global tourism hub imbues these local findings with international significance. The presence of tourists and tourism workers in the cohort is direct clinical evidence of the interface between local and global populations. A gonococcal strain that acquires resistance due to suboptimal treatment in Bali today can be transported across continents tomorrow. The combination of a potentially less effective antibiotic with a near-total absence of follow-up creates a perfect storm: a proportion of patients may experience treatment failure, remain infectious (perhaps asymptomatically), and continue to transmit the pathogen within their diverse sexual networks—networks that are, by the very nature of Bali's economy, both local and international.

This study's primary strength is its provision of rare, real-world data on clinical practices from an under-surveilled and epidemiologically critical region. It moves beyond theoretical risks to document actual treatment patterns and outcomes, highlighting a significant gap between guidelines and frontline care. However, the findings must be interpreted in the context of several important limitations. The most significant limitation of this study is its small sample size (N=58), which was the result of a rigorous screening process that excluded a large number of incomplete records. This small n has several crucial implications. The findings from this single tertiary referral center may not be representative of practices in other healthcare settings in Bali or Indonesia, such as primary care clinics, private practitioners, or facilities specifically catering to key populations. The treatment patterns observed here cannot be assumed to be universal. While some statistically significant differences were found, the study was underpowered to detect more subtle associations. The absence of a significant finding does not confirm the absence of a true effect. The point estimates of prevalence and outcomes are subject to wide confidence intervals, meaning the true population value could be substantially different.¹⁹ Additional limitations include the retrospective design, which is inherently dependent on the accuracy and completeness of

clinical documentation. Data on some variables of interest, such as condom use or specific sexual acts, were too inconsistently recorded to be analyzed. Finally, the absence of culture-based antimicrobial susceptibility testing (AST) data is a major constraint. Our conclusions regarding AMR are based on the inferred risk from suboptimal treatment practices; we cannot report on the actual prevalence of resistant *N. gonorrhoeae* in this cohort.²⁰

5. Conclusion

This study reveals a critical misalignment between the local clinical management of gonorrhoea and evidence-based global standards at a major referral center in Bali, Indonesia. The synergistic failure of using a suboptimal antimicrobial monotherapy and a near-complete inability to retain patients for follow-up poses a significant, unmonitored risk for treatment failure, continued STI transmission, and the amplification of antimicrobial resistance in a region of global epidemiological importance. These findings are not merely an academic observation; they are a call to urgent action. We propose the following urgent public health recommendations. Local and national public health authorities in Indonesia must prioritize the urgent review and alignment of gonorrhoea treatment guidelines with current international standards, specifically advocating for the replacement of cefixime with high-dose injectable ceftriaxone as the first-line empiric therapy. The catastrophic gap in patient follow-up must be addressed through the development and implementation of innovative, culturally sensitive retention strategies. These could include leveraging digital health tools like SMS or WhatsApp reminders, providing patient education on the importance of a test-of-cure, reducing structural barriers by offering free or low-cost follow-up visits, and engaging community health workers. There is an urgent need to establish robust, routine surveillance for gonococcal AMR in Bali and other high-risk areas in Indonesia. This requires investment in laboratory capacity for culture and antimicrobial susceptibility testing, which is essential for tracking resistance trends and

informing future treatment guidelines. Without these decisive interventions, this high-transmission setting risks becoming a significant and active contributor to the global crisis of untreatable gonorrhoea.

6. References

1. Hananta IPY, van Dam AP, Schim van der Loeff MF, Dierdorp M, Wind CM, Soebono H, et al. Molecular epidemiology of *Neisseria gonorrhoeae* strains circulating in Indonesia using multi-locus variable number tandem repeat analysis (MLVA) and *Neisseria gonorrhoeae* multi-antigen sequence typing (NG-MAST) techniques. *BMC Infect Dis*. 2018; 18(1): 7.
2. Pasaribu LR, Puspendari N. Risk factors to gonorrhoea among female sex worker in three cities in Indonesia. *Annals of Tropical Medicine and Public Health*. 2019; 22(11): 274–88.
3. Indriatmi W, Prayogo RL, Nilasari H, Suseno LS. Antimicrobial resistance of *Neisseria gonorrhoeae* in Jakarta, Indonesia: a cross-sectional study. *Sex Health*. 2020; 17(1): 9–14.
4. Hidayati AN, Sawitri, Rositawati A, Wardhani PH, Bintanjoyo L. Susceptibility of *Neisseria gonorrhoeae* against a dual treatment antibiotics regimen in primary health centres in Surabaya, Indonesia. *Aust J Gen Pract*. 2024; 53(7): 499–503.
5. Andualem T, Belay G, Desta AF, Nigussie H, Mulu W, Desalegn A, et al. The burden of *Neisseria gonorrhoeae* infection, risky sexual behavior, and associated risk factors among sexually transmitted infections in a resource-limited setting area of Addis Ababa City, Ethiopia. *Front Reprod Health*. 2025; 7(1601088).
6. Peter M, Saudah N. A systematic review of studies on the resistance of *Neisseria gonorrhoeae* to ciprofloxacin and cefixime. *Preprints*. 2025.
7. Kanesaka I, Abdellati S, Gestels Z, Vanbaelen T, De Baetselier I, de Block T, et al. Nourseothricin as a novel therapeutic agent against *Neisseria gonorrhoeae*: in vitro and in vivo evaluations using *Galleria mellonella*-a pilot study. *Microbiol Spectr*. 2025; 13(8): e0127525.
8. Yu CY, Lim XR, Van Phan T, Mat Isa N, Yean CY, Chan K-G, et al. Advances in molecular diagnostics of *Neisseria gonorrhoeae*. *J Microbiol Methods*. 2025; 236(107197): 107197.
9. Wei X, Huang X, Huang Y, Su T, Duan Q, Wan J, et al. Analyses of Human papillomavirus, *Ureaplasma urealyticum*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, herpes simplex virus 2 and coinfections among male outpatients in Kunming, China. *Diagn Microbiol Infect Dis*. 2025; 113(1): 116896.
10. Priest D, Ong JJ, Chow EPF, Tabrizi S, Phillips S, Bissessor M, et al. *Neisseria gonorrhoeae* DNA bacterial load in men with symptomatic and asymptomatic gonococcal urethritis. *Sex Transm Infect*. 2017; 93(7): 478–81.
11. Al-Madboly L, Gheida S. Case report of urethritis in a male patient infected with two different isolates of multiple drug-resistant *Neisseria gonorrhoeae*. *Front Med (Lausanne)*. 2017; 4: 194.
12. Reddy Dudhipala S, Prasad, Kishore L R, Ramana Godha V, Krishna Ananthula V, Pinjala P, et al. A study of co-infection with *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in male urethritis. *J Evol Med Dent Sci*. 2017; 6(49): 3746–50.
13. Retchless AC, Kretz CB, Chang H-Y, Bazan JA, Abrams AJ, Norris Turner A, et al. Expansion of a urethritis-associated *Neisseria meningitidis* clade in the United States with concurrent acquisition of *N. gonorrhoeae* alleles. *BMC Genomics*. 2018; 19(1): 176.

14. Silva GAR da, Motta HL de SN, Souza EFA de, Cardoso PANM, Pilotto JH, Eyer-Silva WA, et al. Prevalence of asymptomatic urethritis by *Chlamydia trachomatis* and *Neisseria gonorrhoeae* and associated risk factors among males living with HIV-1. *Rev Inst Med Trop Sao Paulo*. 2018; 60.
15. Tshokey T, Tshering T, Pradhan AR, Adhikari D, Sharma R, Gurung K, et al. Antibiotic resistance in *Neisseria gonorrhoea* and treatment outcomes of gonococcal urethritis suspected patients in two large hospitals in Bhutan, 2015. *PLoS One*. 2018; 13(8): e0201721.
16. Rossignol L, Feuillepain L, Ndeikoundam Ngangro N, Souty C, Fournet N, Le Strat Y, et al. Estimate of male urethritis incidences in France between 2007 and 2017 with a specific focus on *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis* infections. *BMC Infect Dis*. 2019; 19(1): 561.
17. Chen S-C, Hu L-H, Zhu X-Y, Yin Y-P. Gonococcal urethritis caused by a multidrug resistant *Neisseria gonorrhoeae* strain with high-level resistance to spectinomycin in China. *Emerg Microbes Infect*. 2020; 9(1): 517–9.
18. Bayirli Turan D, Gümüş D, Kalayci Yüksek F. The Evaluation of Urethritis in Men Caused by *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Ureaplasma urealyticum*, and *Mycoplasma hominis*: Ten-year Retrospective Data from Turkey. *Bezmialem Sci*. 2022; 10(1): 62–7.
19. Yasuda M, Takahashi S, Miyazaki J, Wada K, Kobayashi K, Matsumoto M, et al. The third nationwide surveillance of antimicrobial susceptibility against *Neisseria gonorrhoeae* from male urethritis in Japan, 2016-2017. *J Infect Chemother*. 2023; 29(11): 1011–6.
20. Müller EE, Gumede LYE, Maseko DV, Mahlangu MP, Venter JME, Da Costa Dias B, et al. Emergence of high-level azithromycin-resistant *Neisseria gonorrhoeae* causing male urethritis in Johannesburg, South Africa, 2021. *Sex Health*. 2024; 21(1): NULL.