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Emerging Resistance in *Chlamydia* Requires Surveillance and Reassessment

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ABSTRACT

Background: *Chlamydia trachomatis* remains one of the most common sexually transmitted infections (STIs) globally, often asymptomatic but capable of causing serious reproductive complications if left untreated. While azithromycin and doxycycline have traditionally been highly effective first-line treatments, recent evidence suggests a growing concern over reduced antibiotic efficacy and potential resistance.

Conclusion: This commentary highlights emerging clinical patterns, the need for surveillance, and the importance of reassessing treatment strategies to mitigate a future public health challenge.

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Introduction

Chlamydia has long been considered a treatable Sexually Transmitted Infection (STI), its intracellular nature notwithstanding (1). A single-dose azithromycin or a 7-day course of doxycycline has been the standard treatment for uncomplicated Chlamydia trachomatis infections for decades (2). However, recent reports of treatment failures, particularly associated with azithromycin, raise concerns about emerging resistance and potential shifts in treatment effectiveness (3). Therefore, in an era of growing antimicrobial resistance and increasing global antibiotic consumption, possibility for Chlamydia trachomatis resistance should not be overlooked but rather periodically monitored to ensure we are not caught unprepared (4). Although laboratory-confirmed antibiotic resistance in Chlamydia trachomatis remains difficult to establish-primarily due to its intracellular nature and the lack of reliable culture methods-growing clinical evidence indicates an increasing rate of treatment failure (5). A 2016 published study reported that, azithromycin treatment failure rates ranging from 6.2% to 12.8% (6). Moreover, reduced therapeutic efficacy may arise from antibiotic resistance, often driven by genetic mutations, or from bacterial persistence, where incomplete eradication occurs due to the organism's inherent tolerance to antibiotics (7). Several factors contribute to this phenomenon. First, the widespread and sometimes inappropriate use of macrolides like azithromycin for various infections may exert selective pressure on pathogens, including *Chlamydia trachomatis* (8, 9). Second, inconsistent patient adherence and incomplete partner treatment can lead to reinfection rather than true resistance (10). Additionally, the lack of reliable laboratory assays to detect in vitro resistance in chlamydia presents a diagnostic gap. Unlike gonorrhea or other bacterial STIs, resistance in Chlamydia trachomatis is typically inferred from persistent infection or recurrent positive tests despite confirmed treatment (11). In light of these concerns, a multifaceted response is needed. First, enhanced surveillance efforts by regional and national public health authorities are essential to monitor trends in treatment failure and suspected resistance (4). Furthermore, there is a growing body of evidence suggesting that doxycycline may offer superior efficacy, particularly in asymptomatic or rectal infections, warranting reconsideration of current first-line treatment recommendations in select populations (12). Education remains critical, both for healthcare providers and patients, to reinforce the importance of adherence, appropriate antibiotic use, and partner management to reduce the risk of reinfection. Finally, investment in research particularly in the development of vaccines, which are currently progressing through early clinical stages could ultimately transform chlamydia control strategies and reduce reliance on antibiotics altogether (13, 14)

Conclusion

The threat of antibiotic resistance in Chlamydia trachomatis is still in its early stages, but the warning signs are clear. As with many other pathogens, the window to act proactively is narrow. Continued reliance on a limited number of antibiotics without robust surveillance or alternative therapies puts us at risk of a future where this common infection may no longer be easily curable. A coordinated effort across clinical practice, research, and public health policy is essential to stay ahead of this emerging challenge.

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Ethics approval and consent to participate

This article does not contain any studies with animals performed by any of the authors.

Conflict of interest

The authors declare that they have no conflict of interest.

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