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## **Ceftriaxone Resistance in *Neisseria gonorrhoeae* Associated with the penA-60.001 Allele in Hanoi, Vietnam**

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Antimicrobial resistance in *Neisseria gonorrhoeae* is an urgent global health threat. Ceftriaxone is the only remaining option for empiric monotherapy of gonococcal infections. The prevalence of ceftriaxone resistance in *N. gonorrhoeae* is highest in the Western Pacific region.<sup>1</sup> Many of the *N. gonorrhoeae* infections associated with high minimum inhibitory concentrations (MICs) to ceftriaxone reported recently in the United States, United Kingdom, and Europe, carry the penA-60.001 allele, which is associated with ceftriaxone resistance and was first detected in the Western Pacific region.<sup>2-4</sup>

The Enhanced Gonococcal Surveillance Programme in Cambodia recently reported 38% of 76 urethral isolates collected from 2021-2022 were associated with ceftriaxone MICs 0.125 mg/L or more.<sup>5</sup> Moreover, all of those resistant isolates harbored the penA-60.001 allele. Those findings are alarming and raise questions over whether ceftriaxone resistance and penA-60.001 are more widespread in the region.

From January through December 2023, all isolates at the Hanoi Medical University Hospital in Hanoi, Vietnam were selected for antibiotic susceptibility testing (AST). MICs were interpreted using European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints. All isolates with ceftriaxone MICs 0.125 mg/L or more underwent DNA extraction and subsequent penA-60.001 detection by real-time (RT)-PCR, based on a penA-60.001 PCR previously used for enhanced surveillance in other settings.<sup>2,6</sup>

In total, 243 *N. gonorrhoeae* isolates were cultured, 13 (5%) were non-viable. Of the 230 available isolates, 224 (97%) were obtained from urethral specimens.

Ceftriaxone MICs greater than 0.125 mg/L were found in 64 (28%) and MICs greater than 0.25 mg/L were detected in 50 (22%). The penA-60.001 positivity was 67% (n=39/64) among those with MICs greater than 0.125 mg/L and 62% (n=31/50) among isolates with MICs greater than 0.25 mg/L. All (n=64/64) isolates with ceftriaxone MICs greater than 0.125 mg/L were resistant to cefixime, with MICs of 0.5 mg/L or more, and susceptible to azithromycin (EUCAST epidemiological cut-off  $\leq 1$  mg/L).

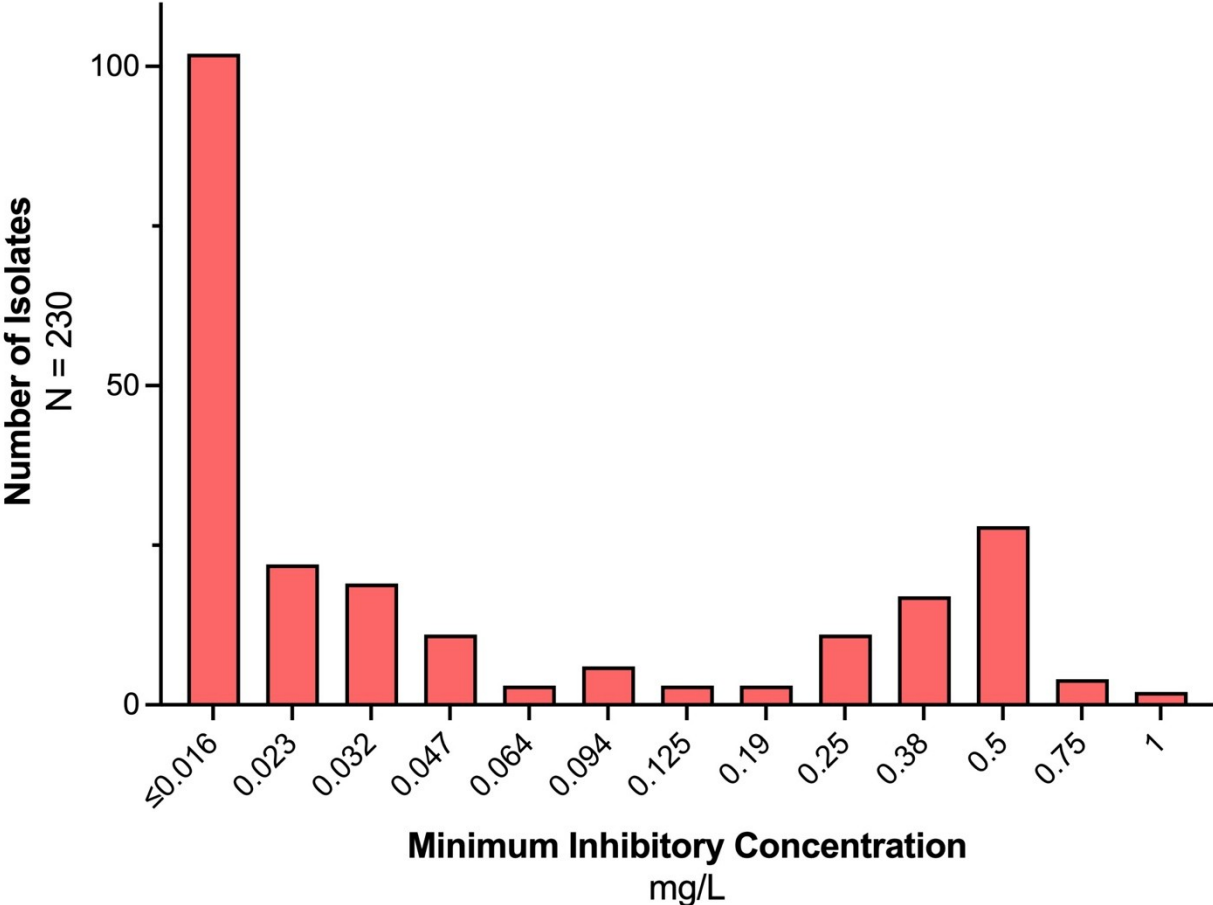
These findings highlight the troublingly high prevalence of ceftriaxone resistance in the Western Pacific region, with more than a quarter of *N. gonorrhoeae* isolates being resistant to first-line therapy in this setting, and that strains harboring penA-60.001 are becoming increasingly prevalent in the Western Pacific region. Our report underscores the utility of direct detection of penA-60.001, which could be used to rapidly detect resistance and might prove to be a useful surveillance tool more widely. The findings also suggest the presence of non-penA-60.001 mutations contributing to ceftriaxone resistance in this setting. Further analyses with whole genome sequencing and multilocus sequence typing would help to elucidate those resistance mutations and better understand their transmission dynamics.

Ceftriaxone as first-line therapy for gonorrhoea is under threat and interventions are urgently needed to improve the detection of resistance and to mitigate further transmission.

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**Figure 1.** Distribution of ceftriaxone minimum inhibitory concentrations (MICs) for 230 *N. gonorrhoeae* isolates from Hanoi, Vietnam.



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