Prevalence of cefixime-resistant *Neisseria gonorrhoeae* in Melbourne, Australia, 2021-2022

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Background:
The rise of antimicrobial-resistant *Neisseria gonorrhoeae* is a global health threat. While ceftriaxone remains the first-line treatment for *N. gonorrhoeae*, the US CDC has recommended cefixime as a second-line treatment; however, cefixime is not currently available in Australia. This study aimed to examine the prevalence of cefixime-resistant *N. gonorrhoeae* among individuals attending a sexual health clinic in Melbourne, Australia.

Methods:
We conducted a cross-sectional study among individuals attending the Melbourne Sexual Health Centre between 9-August-2021 and 18-July-2022. We included individuals with culture-confirmed *N. gonorrhoeae* where their isolates underwent antimicrobial susceptibility testing for cefixime, azithromycin and ceftriaxone. Multivariable logistic regression with a generalised estimating equation was performed to examine the factors associated with cefixime-resistant *N. gonorrhoeae.*

Results:
A total of 1176 *N. gonorrhoeae* isolates were included. The prevalence of cefixime resistance was 6.3%, azithromycin resistance was 4.9% and ceftriaxone resistance was 0%. Cefixime resistance was the highest among women (16.4%, 10/61), followed by men who have sex with women (6.4%, 7/109), men who have sex with men (6.0%, 65/1090) and gender-diverse people (0%, 0/24) (p=0.006). However, cefixime resistance did not differ across anatomical sites (genital, oropharyngeal and anorectal) (p=0.568). Multivariable logistic regression showed that women (adjusted odds ratio [aOR]=2.75, 95% CI: 1.23-6.11) had higher odds of having cefixime-resistant *N. gonorrhoeae*. Age, HIV status, PrEP use, sex workers, and having

partners from overseas in the past 12 months were not associated with cefixime-resistant *N. gonorrhoeae*.

Conclusion:
The prevalence of cefixime-resistant *N. gonorrhoeae* among sexually-active individuals in Melbourne exceeds the maximum 5% resistance rate, particularly in women, recommended by WHO for using an antimicrobial as a standard treatment regime. Thus, cefixime treatment may have limited benefits in Australia, particularly in certain population groups. Future work should characterise cefixime-resistant lineages circulating in our setting.

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