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# Antimicrobial susceptibility and molecular epidemiology of *Neisseria gonorrhoeae* infection in East London, South Africa

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## Background

- Antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* is emerging worldwide and a major public health concern
- There is a paucity of *N. gonorrhoeae* AMR data from sub-Saharan Africa because diagnostic testing and resistance surveys are not routinely available
- This study aimed to conduct a comprehensive phenotypic and genotypic evaluation of the AMR profile of *N. gonorrhoeae* isolates in South Africa

## Methods

- We collected 100 *N. gonorrhoeae* isolates from men with urethral discharge syndrome (n=89) and women with vaginal discharge syndrome (n=11) at five primary healthcare facilities in East London, South Africa
- On-site Xpert<sup>®</sup> CT/NG testing was performed and discharge swabs were processed for culture in case of positive Xpert<sup>®</sup> result for *N. gonorrhoeae*
- Swabs were directly inoculated on New York City agar followed by same-day transport to the laboratory
- Growth was identified using Gram-stain, oxidase testing and API-NH<sup>®</sup> strips followed by antimicrobial susceptibility testing by E-test<sup>®</sup> using EUCAST breakpoints
- Whole genome sequencing (WGS) was done on all isolates

Table 1. Antimicrobial susceptibility profiles and MICs for *Neisseria gonorrhoeae* isolates collected from symptomatic individuals in the Eastern Cape province, South Africa, 2022

Drug	Number of isolates (%) <sup>a</sup>			MIC (mg/liter)	
	Susceptible	Intermediate	Resistant	Median (MIC <sub>50</sub> )	Range
Azithromycin	99 (99%)	0	1 (1%)	0.064	0.016 – 8.0
Cefixime	100 (100%)	0	0	0.016	0.016 – 0.064
Ceftriaxone	100 (100%)	0	0	0.016	0.016
Ciprofloxacin	24 (24%)	3 (3%)	73 (73%)	0.50	0.002 – 32
Penicillin	28 (28%)	31 (31%)	41 (41%)	0.25	0.016 – 256
Spectinomycin	100 (100%)	0	0	4.0	0.064 – 16
Tetracycline	25 (25%)	0	75 (75%)	8.0	0.016 – 64

<sup>a</sup>EUCAST breakpoints were used to classify isolates as susceptible, intermediate, or resistant.

The epidemiological cut-off of 1.0 mg/liter was used for azithromycin as no breakpoint are available.

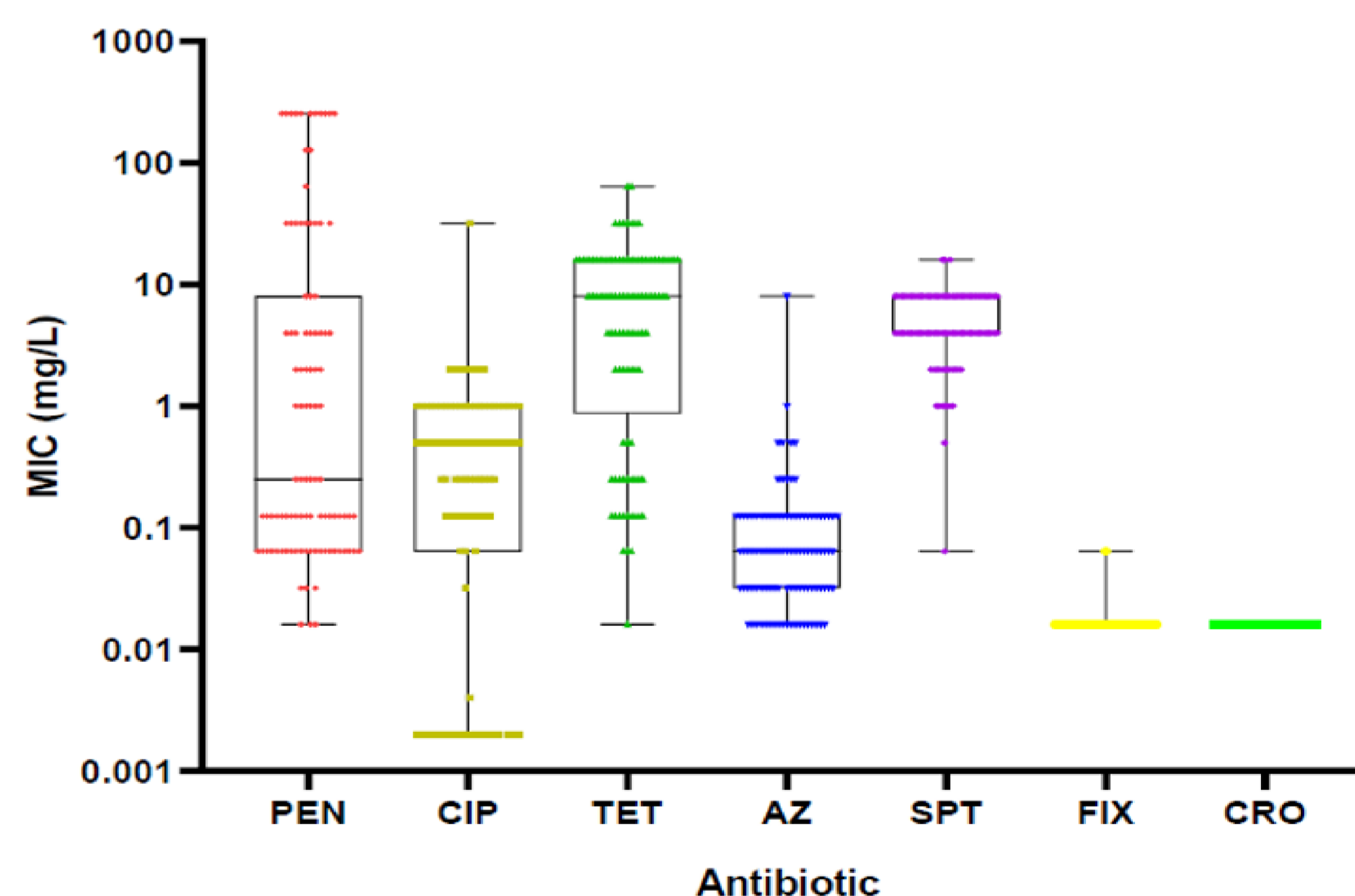
Table 2. Resistance-associated mutations *Neisseria gonorrhoeae* isolates (n=99) non-susceptible to ciprofloxacin, penicillin and tetracycline from the Eastern Cape province, South Africa

Antibiotic	Gene	Mutation	Number of isolates with mutation
Ciprofloxacin (n=75) (MIC > 0.03 mg/liter)	<i>gyrA</i>	S91F	70 (93%)
	<i>gyrA</i>	D95G	24 (32%)
	<i>gyrA</i>	D95A	46 (61%)
	<i>parC</i>	D86N	19 (25%)
	<i>parC</i>	S87N	30 (40%)
	<i>parC</i>	E91K	2 (3%)
Penicillin G (n=71) (MIC > 0.06 mg/liter)	<i>bla<sup>TEM</sup></i>	-	46 (65%)
	<i>mtrR</i>	A39T	31 (44%)
	<i>penA</i>	ins346D	71 (100%)
	<i>ponA1</i>	L421P	35 (49%)
Tetracycline (n=74) (MIC > 0.5 mg/liter)	<i>tetM</i>	-	72 (97%)
	<i>rpsJ</i>	V57M	69 (93%)
	<i>mtrR</i>	A39T	35 (47%)

## Results

- Most isolates showed reduced susceptibility or resistance to ciprofloxacin (76%), penicillin (72%), and tetracycline (75%), but not to cefixime or ceftriaxone (Table 1).
- One strain had a minimum inhibitory concentration (MIC) for azithromycin (8.0 mg/L) above the epidemiological cut-off; other strains had MIC values of 1.0 mg/L (n=1), 0.50 mg/L (n=4), 0.25 mg/L (n=5) and lower (Figure 1)
- WGS was successful for 99 isolates; known resistance-associated mutations were identified (Table 2).
- WGS showed 86 isolates that belonged to 56 novel NG-MAST types, 12 strains to 10 known types, and two that were mixed
- Phylogenetic analysis revealed a geographically diverse, well-established epidemic with several clusters

Figure 1. Medium Inhibitory Concentration distribution of 100 *Neisseria gonorrhoeae* isolates from the Eastern Cape province, South Africa, 2022



## Conclusions

- Our data confirm extensive AMR in *N. gonorrhoeae* to ciprofloxacin, penicillin and tetracycline in South Africa
- The low MICs of *N. gonorrhoeae* for the cephalosporin drugs is reassuring and confirms use of ceftriaxone and cefixime in syndromic management of STIs
- One case of high-level azithromycin resistance was detected; this highlights the importance of ongoing surveillance to monitor the situation
- The observed high frequency of novel NG-MAST types adds to global *N. gonorrhoeae* genomics data, and highlights the importance of conducting geographically widespread studies when evaluating novel diagnostic tests and therapeutic options