Molecular Characterization of Antimicrobial Resistance Genes in *Neisseria gonorrhoeae* in Southeast Michigan

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Background

- Antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* (NG) is a public health crisis.
- Diagnosis is primarily established using nucleic acid amplification technologies (NAATs) without susceptibility testing; thus, rapid identification of resistance determinants is crucial.
- Whole-genome sequencing (WGS) is a promising alternative to current susceptibility methods.
- The purpose of this study was to describe AMR genes in NG isolates using WGS from Southeast Michigan.

Methods

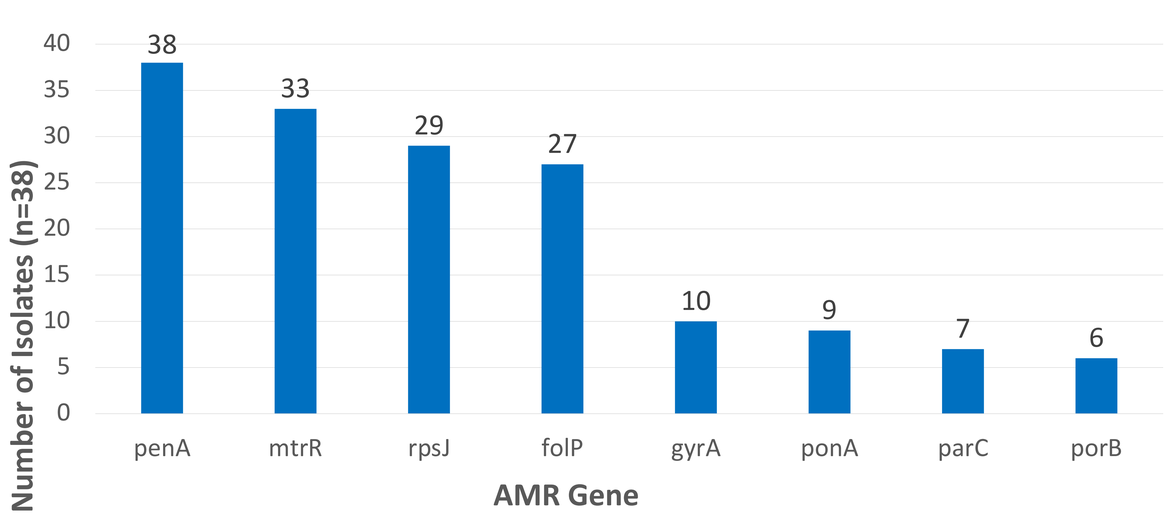
- Isolates, demographic data, and minimum inhibitory concentrations (MIC) via E-test (ceftriaxone/CRO) and broth microdilution (azithromycin/AZM) were obtained from the Michigan Department of Health and Human Services.
- Libraries from isolates were generated using QIAseq FX DNA library kit before sequencing on NovaSeq 6000.
- Reads were trimmed [Trimmomatic] and aligned to the NG genome [Burroughs-Wheeler Aligner] before processing with Samtools suite for variant detection and consensus WGS determination.
- AMRFinderPlus was used to categorize AMR genes and resistance-associated point mutations.

Results

Table 1. Clinical characteristics of patients

Characteristic	Number (%) (n=38)
HIV status	
- Positive	6 (15.7%)
- Negative	11 (28.9%)
- Unknown	21 (55.2%)
Sexual orientation	
- Female having sex with males	14 (44.7%)
- Male having sex with females and males	2 (5.2%)
- Male having sex with males	4 (10.5%)
- Unknown	18 (47.3%)
Previous NG infection	
- More than once	5 (13.2%)
- Once	8 (21%)
- No	25 (65.8%)
Previous other sexually transmitted infection	
- More than once	9 (23.7%)
- Once	5 (13.1%)
- No	24 (63.2%)
Specimen source	
- Blood	1 (2.6%)
- Urine	18 (47.3%)
- Cervix, vagina	11 (28.9%)
- Throat	3 (7.9%)
- Perianal, rectal	3 (7.9%)
- Penis	1 (2.6%)

Figure 1. Presence of AMR genes among isolates



Legend: penA = cephalosporin resistance through penicillin-binding protein 2; mtrR = multidrug (macrolide/beta-lactam/tetracycline) efflux system transcriptional repressor; rpsJ = tetracycline resistance through 30S ribosomal protein; folP = sulfonamide resistance through dihydropteroate synthase; gyrA = quinolone resistance through DNA gyrase subunit A; ponA = beta-lactam resistance through penicillin binding protein 1; parC = quinolone resistance through DNA topoisomerase IV subunit A; porB = beta-lactam resistance through major outer membrane protein porin P

Results

- Total of 38 isolates from different patients were analyzed; the majority were from males (63%) and Black race (44.7%) living in Detroit City proper (47.3%) with median age 25 (range 13-56), unknown HIV status (55.2%) and sexual orientation (47.3%) (Table 1).
- Urine (47.3%) was the most common source, followed by cervix/vagina (28.9%).
- More than a third had prior NG and other sexually transmitted infections.
- Eight resistance genes were found among the 38 isolates (Figure 1).
  - –penA gene associated with cephalosporin resistance was found in all isolates; however, all isolates were susceptible to CRO (CLSI susceptible breakpoint MIC $\leq$ 0.25).
  - –mtrR gene associated with macrolide resistance was noted in 86.8% isolates; however, resistance was noted in 9 (27%) of 33 isolates where AZM susceptibility testing was available (CLSI resistance breakpoint MIC $\geq$ 1).

Conclusions

- We describe a potential utility for WGS to identify antimicrobial resistance genes in *Neisseria gonorrhoeae*.
- Although numerous β-lactam resistance genes were detected in all isolates, all remained susceptible to ceftriaxone.
- Further research is needed to determine the extent to which genetic diversity affects phenotypic susceptibilities in *Neisseria gonorrhoeae*.

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