Increased Prevalence of Group A Streptococcus (GAS) high level macrolide resistance during the COVID-19 Pandemic

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Background/Objectives

- COVID-19 has affected the epidemiology of many respiratory pathogens including Group A Streptococcus (GAS).
- Assessing genetic heterogeneity (*emm* type, antimicrobial resistance, virulence factors) can inform treatment recommendations and targets for potential GAS vaccines.
- We assessed GAS clinical antibiotic susceptibility and performed whole genome sequencing (WGS) among pediatric pharyngeal isolates from 2020–2022.

Methods

- We created an outpatient surveillance network for GAS in Chicago, IL; Atlanta, GA; Portland, OR; and Phoenix, AZ.
- From 1/2020–3/2022 throat swabs were collected from children aged 3-18 years in pediatric clinics and EDs from:
  - 1) children with acute GAS pharyngitis by rapid test and
  - 2) among a convenience sample of asymptomatic children to assess for GAS colonization
- Swabs were plated on blood agar and GAS confirmed
- Clinical susceptibility to erythromycin (ERY) and ciprofloxacin (CIP) was assessed by E-test.
- *emm* type and antimicrobial resistance genes (for ERY, Clindamycin (CLI), and fluroquinolones) were assessed by WGS.

Results

- ***Specimen collection:***
  - 1144 pharyngeal swabs were collected:
    - 684 from children with pharyngitis
      - 359/684 (52%) yielded GAS on culture
    - 460 from asymptomatic children
      - 20/460 (4.3%) yielded GAS on culture

- ***Phenotypic resistance via E-test performed on 364 isolates:***
  - 55/364 (15%) tested isolates were ERY resistant and 5/364 (1.4%) CIP resistant
  - The proportion of isolates with ERY resistance increased significantly from 2020 (6%) to 2021–2022 (25%) (c^2 = 23.70, p<.00001) **(Figure 1)**.
  - MICs were high among ERY resistant GAS **(Table 1)**.

- ***Genotypic resistance via WGS:***
  - Of 304 sequenced GAS isolates:
    - 40/304 (13%) were ERY resistant,
    - 35/304 (11.5%) were both ERY resistant and CLI (inducible or constitutive) resistant
    - 4/304 (1.3%) fluoroquinolone resistant
  - Among the 20 isolates from asymptomatic children no ERY, CLI, or CIP resistance occurred, and no resistance genes were identified.
  - *erm*B (62%) was the most common gene for ERY resistance and constitutive CLI resistance, followed by *erm*TR (23%) and *erm*T (11%) both conferring inducible CLI resistance
  - The *emm* types associated with ERY and CLI resistance were *emm*11, 9, 77, 58, and 94.

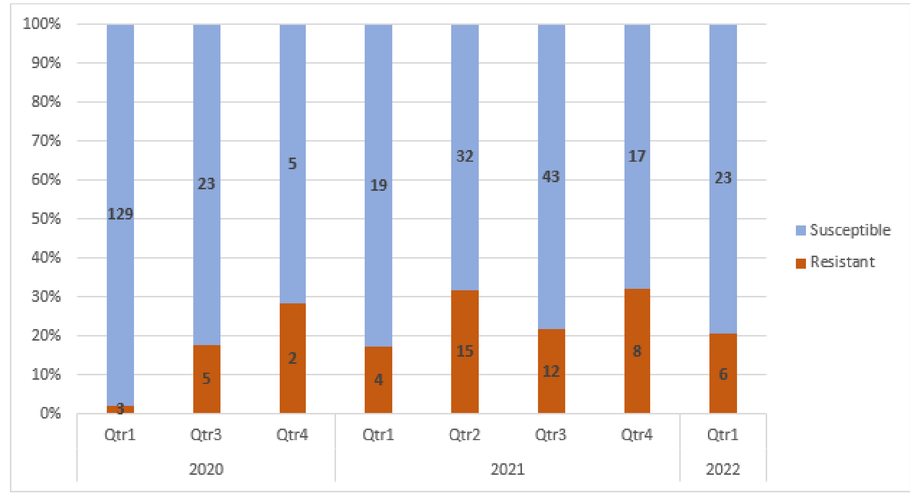

Figure 1. Proportion of tested isolates from children with GAS pharyngitis (N= 346) with phenotypic erythromycin resistance (MIC ≥ 1 µg/mL) per quarter from 2020 to 2022. An increase in the proportion of isolates resistant to erythromycin by E-test was found in 2021–2022 compared to 2020. The data demonstrate an increase in phenotypic erythromycin resistance starting in Qtr3 of 2020. Note: Pandemic-related research pause occurred in 2020 Qtr2 (March 20 – June 24).

Table 1. Minimum Inhibitory Concentration (MIC) values of erythromycin (ERY) and clindamycin (CLI) resistant GAS isolates. Most resistant isolates demonstrated high MICs. 28/55 (51%) of ERY resistant isolates had MIC ≥256.

Antibiotic	# isolates	Median MIC (µg/mL)	Range	Interquartile range
Erythromycin (ERY)	55	≥256	1 to ≥256	3 to ≥256

Conclusions

- ERY resistance increased from 2020–2022.
- The high rate of CLI resistance among ERY resistant GAS was associated with *erm* genes.
- **Implications:** These results are important to inform treatment recommendations for GAS pharyngitis and targets for vaccine development that can reduce antimicrobial-resistant GAS disease.