Analysis of Co-Resistance Among *Klebsiella pneumoniae* Urine Isolates From Female Outpatients in the United States

Keith S. Kaye[1], Vikas Gupta[2], Aruni Mulgirigama[3], Ashish V. Joshi[4], Nicole E. Scangarella-Oman[4], Kalvin Yu[2], Janet Watts[2], Fanny S. Mitrani-Gold[4]

[1]Rutgers - Robert Wood Johnson Medical School, New Brunswick, NJ, USA; [2]BD (Becton, Dickinson and Company), Franklin Lakes, NJ, USA; [3]GSK, Surrey, UK; [4]GSK, Collegeville, PA, USA

Introduction

- Extended-spectrum β-lactamase-producing (ESBL+) Enterobacterales are listed as a serious health threat, according to the Centers for Disease Control and Prevention antimicrobial resistance (AMR) Threats Report (2019)[1]
- While the clinical epidemiology of uncomplicated urinary tract infections (uUTI) has remained relatively stable in recent years, there has been a notable increase in AMR and multi-drug resistance (MDR) among uropathogens in outpatient uUTIs, including ESBL+ Enterobacterales[2–4]
- Urine cultures are seldom ordered for uUTI (33% and 40% in Spain and UK, respectively), therefore surveillance data are limited[5]
- The purpose of the study was to evaluate *Klebsiella pneumoniae* (*K. pneumoniae*) urine culture isolates, from female outpatients in the United States (US) for co-resistance (AMR to 2, 3, and 4 drug classes)

Methods

- This was a retrospective, cross-sectional study of 30-day non-duplicate *K. pneumoniae* urine culture isolates from female outpatients with presumed uUTI (≥ 12 years of age) at 304 US facilities
- Eligible patients had ≥ 3 months of data from 2011–2019, recorded in the BD (Becton, Dickinson and Company) Insights Research Database (Franklin Lakes, NJ, USA)
- Index non-susceptible (NS) *K. pneumoniae* isolates from urine cultures were defined as follows:
  - ESBL+ by a commercial panel or NS (intermediate/resistant) to ceftriaxone, cefotaxime, ceftazidime, or cefepime
  - NS to any of: fluoroquinolones (FQs), trimethoprim/sulfamethoxazole (SXT), or nitrofurantoin (NFT)[6]
- Microbiological co-resistance phenotypes were characterized in isolates NS to 2, 3, and 4 of the resistance phenotypes assessed
- Results are presented for all combinations of co-resistance evaluated, when starting with one resistance phenotype

References

1. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States 2019. Available from: https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf. Accessed: July 15, 2022.
2. Chen HE, et al. *Antibiotics* 2020;9(8):E50.
3. Frazee BW, et al. *Ann Emerg Med* 2018;72(4):449–56.
4. Lob SH, et al. *Diagn Microbiol Infect Dis* 2016;85(4):459–65.
5. Ganzeboom KMJ, et al. *Prim Health Care Res Dev* 2018;20:1–8.
6. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. M100 32nd Edition. CLSI Guidelines. M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2022.

- **Among non-duplicate outpatient (30-day) *K. pneumoniae* urine culture isolates with identified starting resistance (Table):**
  - **70–80% of isolates (ESBL+, FQ NS, and SXT NS) demonstrated co-resistance to NFT NS**
  - **65.7% of ESBL+ isolates demonstrated co-resistance to SXT NS**
  - **54.0% of FQ NS isolates demonstrated co-resistance to SXT+NFT, with 45.7% of ESBL+ isolates also FQ NS+SXT NS**

Table. Co-resistance Phenotype Combinations Observed Among *K. pneumoniae* Isolates From Urine (2011–2019)

Starting resistance phenotype, n (%)		ESBL+	FQ NS	SXT NS	NFT NS	FQ NS + SXT NS	FQ NS + NFT NS	SXT NS + NFT NS	NS to all 4 phenotypes
ESBL+	11,065 (100)		6077 (54.9)	7266 (65.7)	8356 (75.5)	5061 (45.7)	4987 (45.1)	5770 (52.2)	4228 (38.2)
FQ NS	10,962 (100)	6077 (55.4)		7197 (65.7)	8722 (79.6)			5916 (54.0)	4228 (38.6)
SXT NS	23,887 (100)	7266 (30.4)	7197 (30.1)		16,640 (69.7)		5916 (24.8)		4228 (17.7)
NFT NS	141,545 (100)	8356 (5.9)	8722 (6.2)	16,640 (11.8)		5916 (4.2)			4228 (3.0)

Note: 250,719 non-duplicate (30-day) *K. pneumoniae* isolates (with at least 1 resistance phenotype) were evaluated. Some isolates had overlapping susceptibilities/antimicrobial resistance types, hence individual phenotype totals do not reflect total number of isolates evaluated. The categories are not mutually exclusive as the isolates are grouped based on the phenotype observed.

Please find the online version of this poster and accompanying audio by scanning the QR code or via http://tago.ca/_idw2

Results

- Among the 250,719 non-duplicate *K. pneumoniae* urine culture isolates (with at least 1 resistance phenotype) evaluated for co-resistance, 4.4% were ESBL+; 4.4%, 9.5%, and 56.5% were NS to FQ, SXT, and NFT, respectively
- Of ESBL+ isolates (11,065), 54.9% were co-resistant to FQ, 65.7% to SXT, and 75.5% to NFT (Table)
  - Of the ESBL+ isolates, 45.7% were co-resistant to FQ+SXT, 45.1% to FQ+NFT, and 52.2% to SXT+NFT
  - 38.2% of ESBL+ isolates demonstrated co-resistance to all 4 phenotypes
- For FQ NS isolates (10,962), 55.4% were also ESBL+, 65.7% were co-resistant to SXT, and 79.6% to NFT
  - Of the FQ NS isolates, 54.0% were co-resistant to SXT+NFT
  - 38.6% of FQ NS isolates demonstrated co-resistance to all 4 phenotypes
- Among SXT NS isolates (23,887), 30.4% were also ESBL+, 30.1% were co-resistant to FQ, and 69.7% to NFT
  - Of the SXT NS isolates, 24.8% were co-resistant to FQ+NFT
  - 17.7% of SXT NS isolates demonstrated co-resistance to all 4 phenotypes
- For NFT NS isolates (141,545), 5.9% were ESBL+, 6.2% were co-resistant to FQ, and 11.8% to SXT
  - Of the NFT NS isolates, 4.2% were co-resistant to FQ+SXT
  - 3.0% of NFT NS isolates demonstrated co-resistance to all 4 phenotypes

Conclusions

- The data from this study demonstrate the high rates of co-resistance in isolates that are already resistant to one antibiotic, and indicate that the availability of effective oral treatments for uUTI are limited by antibiotic resistance
- These findings can be used to help inform appropriate empiric prescribing practices to optimize the treatment of uUTI, and highlight a key need for appropriate treatment of patients with uUTI in the future
- It is crucial to raise awareness among clinicians about the current patterns of AMR to appropriately inform their treatment decisions and effectively serve their patients

Disclosures

KSK has previously received symposia honoraria from GSK. VG, KY, and JW are employees of BD (VG and KY are shareholders), which received funding from GSK to conduct this study. AM, AVJ, NES-O, and FSM-G are employees of, and shareholders in, GSK. GSK sponsored study 212502. On behalf of all authors, an audio recording of this poster was prepared by KSK, who did not receive any payment for this presentation. Medical writing support for the development of this poster, associated audio script, and abstract, under direction of the authors, was provided by Suzan Maboane, MSc, and Fraser Shearer, PhD, of Ashfield MedComms, an Inizio company, and funded by GSK.

Presentation number: 2226, Session: UTIs
IDWeek 2022 | October 19–23, 2022 | Washington, DC, USA