

Household (HH) outbreak of ESBL-producing *Escherichia coli* sequence type 131 (ST131) infection with high rate of ST131 intestinal colonization and extensive strain sharing among HH members

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Abstract

Background: Reasons for the successful global dissemination of multi-drug resistant *E. coli* ST131 are undefined, but may include enhanced transmissibility or ability to colonize the intestine compared to other strains. Accordingly, we assessed the prevalence of ST131 intestinal colonization among HH members of an infant with recurrent urinary tract infections (UTIs) caused by an ESBL-producing, fluoroquinolone resistant (FQ-R) ST131 *E. coli* strain.

Methods: *E. coli* was isolated from urine (index patient only) and fecal specimens from all 7 HH members, including the index patient, 3 older siblings, 2 parents, and 1 dog. Isolates were characterized by SNP PCR to detect ST131 and its (ESBL-associated) H30-Rx subtype, pulse-field gel electrophoresis to resolve unique strains, and FQ resistance testing.

Results: The index patient, a formerly preterm infant with history of admission to the neonatal intensive care unit presented at 40 days of life with an ESBL-producing *E. coli* UTI. Despite appropriate therapy and no evidence of vesicoureteral reflux or genitourinary abnormalities, she developed three recurrences of ESBL *E. coli* UTI over the next 3 months. During this period, a 2-year-old sister was also diagnosed with ESBL *E. coli* UTI. The index patient's urine isolate represented pulsotype 903 of the FQ-R, ESBL-producing H30-Rx subclone of *E. coli* ST131. The same ST131 strain was identified in fecal samples from the index patient and 4 other asymptomatic human HH members at the initial sampling, and from the index patient and 4 other HH members at a second sampling 10 weeks later. In addition, 2 pulsotypes of FQ-susceptible non-ST131 *E. coli* were each shared by two HH members.

Conclusions: In this HH outbreak investigation of ESBL-producing ST131 UTI, clinical and colonizing isolates of ST131 represented the same strain, and nearly all HH members had ST131 intestinal colonization for several months. These findings suggest that ST131 *E. coli* is an efficient and persistent colonizer that can be easily transmitted within HHs, including among children. Strategies to prevent ST131 spread within the community are urgently needed.

Study aim

To determine the prevalence of colonization with ESBL-producing ST131 *E. coli* among HH members of the index patient, a 40 day old female with recurrent ST131 UTIs.

HH colonization with *E. coli* over three fecal sampling rounds

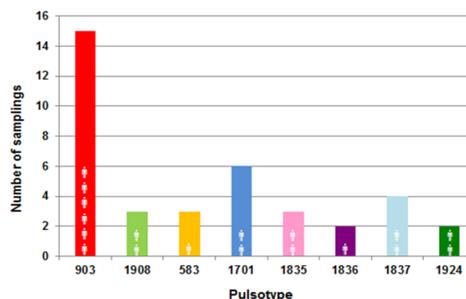
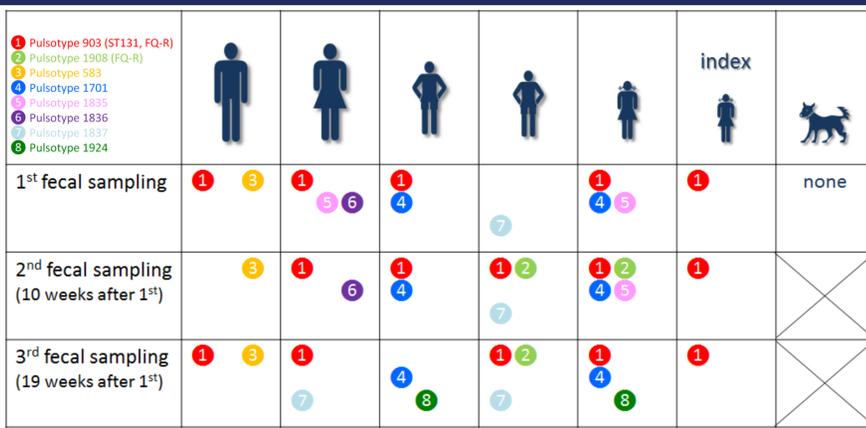


Figure and bar chart displaying HH colonization with eight different identified pulsotypes.

The top figure shows the pulsotypes found among different HH members during three fecal sampling rounds.

The bar chart on the bottom quantifies the presence of pulsotypes during all sampling rounds. The figures within the bars show how many HH members carried the pulsotype over the entire study period.

Antibiotic resistance

Antibiotic	Pulsotype resistance to listed antibiotic*							
	ST131 903 n=15	1908 n=3	583 n=3	1701 n=6	1835 n=3	1836 n=2	1837 n=4	1924 n=2
Ampicillin	Dark	Light	Light	Light	Light	Light	Light	Light
Piperacillin	Dark	Light	Light	Light	Light	Light	Light	Light
Amoxicillin-clavulanic acid	Dark	Light	Light	Light	Light	Light	Light	Light
Piperacillin-tazobactam	Dark	Light	Light	Light	Light	Light	Light	Light
Ampicillin-sulbactam	Dark	Light	Light	Light	Light	Light	Light	Light
Cefepime	Dark	Light	Light	Light	Light	Light	Light	Light
Ceftriaxone	Dark	Light	Light	Light	Light	Light	Light	Light
Cephalothin	Dark	Light	Light	Light	Light	Light	Light	Light
Cefazolin	Dark	Light	Light	Light	Light	Light	Light	Light
Cefotaxime	Dark	Light	Light	Light	Light	Light	Light	Light
Ceftazidime	Dark	Light	Light	Light	Light	Light	Light	Light
Aztreonam	Dark	Light	Light	Light	Light	Light	Light	Light
Gentamicin	Dark	Light	Light	Light	Light	Light	Light	Light
Streptomycin	Dark	Light	Light	Light	Light	Light	Light	Light
Tetracycline	Dark	Light	Light	Light	Light	Light	Light	Light
Ciprofloxacin	Dark	Light	Light	Light	Light	Light	Light	Light
Levofloxacin	Dark	Light	Light	Light	Light	Light	Light	Light
Nalidixic acid	Dark	Light	Light	Light	Light	Light	Light	Light
Trimethoprim	Dark	Light	Light	Light	Light	Light	Light	Light
Trimethoprim-sulfamethoxazole	Dark	Light	Light	Light	Light	Light	Light	Light
Chloramphenicol	Dark	Light	Light	Light	Light	Light	Light	Light
ESBL	Dark	Light	Light	Light	Light	Light	Light	Light
Resistance score** of individual isolates	16-19	15-16	0	0-2	1-2	0-1	0	0-1

*Dark box: ≥ 50% of tested isolates were resistant or intermediate to tested antibiotic
 *Light box: ≤ 50% of tested isolates were resistant or intermediate to tested antibiotic
 **calculated as total number of antibiotics to which isolates were resistant or intermediately susceptible out of 26 tested antibiotics
 All tested isolates were susceptible to cefoxitin, ertapenem, imipenem, amikacin and nitrofurantoin.

Methods

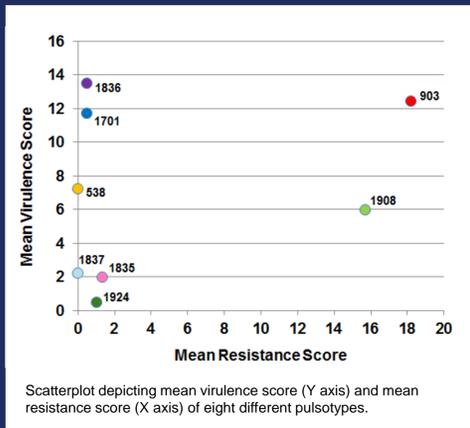
- Fecal samples were obtained from all HH members including the index patient, her parents, three healthy siblings and the family dog. Sampling was repeated after 10 and 19 weeks
- All *E. coli* isolates were characterized by SNP PCR to detect ST131 and pulse-field gel electrophoresis (PFGE) to resolve unique pulsotypes.
- Full antibiotic susceptibility testing via disk diffusion and virulence factor gene analysis was performed on each *E. coli* isolate.

Virulence Factors

Virulence Factor	Pulsotypes with listed virulence factor *							
	ST131 903 n=15	1908 n=3	583 n=3	1701 n=6	1835 n=3	1836 n=2	1837 n=4	1924 n=2
Adhesins								
<i>papAH</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>papC</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>papEF</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>papG</i>	Light	Light	Light	Light	Light	Light	Light	Light
allele II	Light	Light	Light	Light	Light	Light	Light	Light
allele III	Light	Light	Light	Light	Light	Light	Light	Light
<i>sfa/focDE</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>focG</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>afa/draBC</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>iha</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>fimH</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>hlyD</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>hlyE</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>cnf1</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>sat</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>pic</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>vat</i>	Light	Light	Light	Light	Light	Light	Light	Light
Toxins								
<i>iroN</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>fyuA</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>ireA</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>iutA</i>	Light	Light	Light	Light	Light	Light	Light	Light
Siderophore								
<i>kpsM II</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>K1</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>K5</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>usp</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>traT</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>ompT</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>H7 fljC</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>malX</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>clbB</i>	Light	Light	Light	Light	Light	Light	Light	Light
<i>clbN</i>	Light	Light	Light	Light	Light	Light	Light	Light
Misc								
Virulence score** of individual isolates	12-13	6	7.25	10-13	2	12-15	2-3	1

*calculated as sum of virulence factors present among 25 genes tested, not including *Gi*, *GII*, *GIII*, *sfas*, *focG*, *K1*, *K5*, *K15*, *K2*, and *clbN* and adjusted for multiple detection of *pap* genes.

Resistance vs. Virulence Score

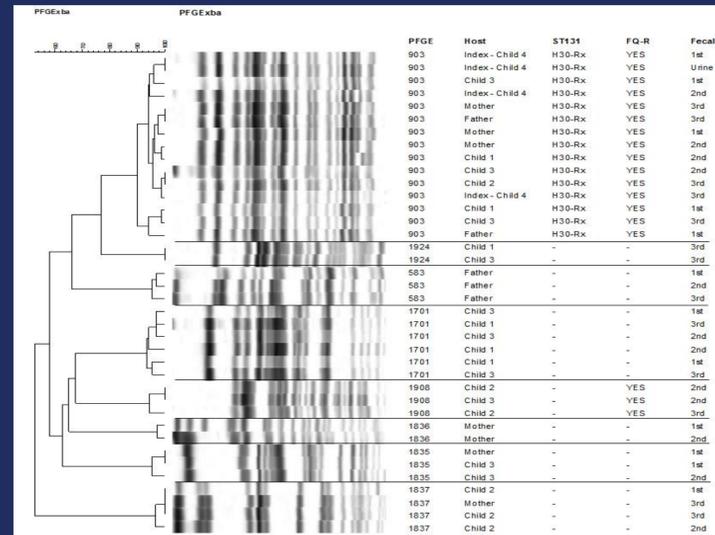


Scatterplot depicting mean virulence score (Y axis) and mean resistance score (X axis) of eight different pulsotypes.

Discussion

- ESBL-producing FQ resistant *E. coli* ST131, pulsotype 903, was the most widely shared and persistent strain in the HH, colonizing 5 HH members at 3 separate samplings over nearly 5 months, and appearing in 15/18 different samplings.
- In contrast, all non-ST131 pulsotypes were found in only 1-2 HH members at a time.
- ST131 903 was the only pulsotype with both high virulence and resistance scores.
- The success of ST131 pulsotype 903 does not appear to be due to its drug resistance or virulence factor profiles alone; pulsotypes with similar resistance (1908) or virulence scores (1701) were not shared as extensively within the HH.

Dendrogram



Dendrogram of PFGE profiles showing relatedness of *E. coli* isolates obtained from a urine sample of the index patient and fecal samples of all HH members on three different sampling occasions. Eight different pulsotypes were found over the three sampling rounds. Pulsotype 903 represents *E. coli* ST131, an ESBL-producing FQ-resistant strain found among all HH members.

Conclusions

- ST131 *E. coli* is an efficient and persistent intestinal colonizer that can easily spread within a HH.
- Persistence and extensive strain sharing among close contacts may contribute to recurrent infections with ST131 *E. coli*.
- Research investigating the molecular basis of ST131's persistence and transmission is needed in order to devise new strategies to treat ST131 and prevent its spread within the community.