Prevalence of CC131 and the Emergence of Other Sequence Types among Escherichia coli Isolates Causing Urinary Tract Infections from Asia-Pacific, Europe, and Latin America

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Introduction

- E. coli is the most common urinary tract pathogen worldwide, implicated in more than a third of all infections in over 20 years of SENTRY Antimicrobial Surveillance Program.
- Many urinary tract infections (UTIs) are community-acquired and empirically treated, hence a good sample of phylogenetic structures and resistance patterns among the causative agents can be obtained.
- The extraintestinal lineage of pathogenic Escherichia coli belonging to clonal complex (CC) 131 has emerged as a multidrug-resistant (MDR) high-risk clone worldwide.
- CC131 is present in approximately 60% of UTI isolates in the US, but its prevalence remains underreported outside the US (ExUS).
- This study evaluated the epidemiology of SENTRY Program ExUS E. coli isolates that met the MIC criteria for the screening of extended spectrum beta-lactamases (ESBLs) and were responsible for UTIs.

Materials and Methods

- A total of 1,161 UTI E. coli isolates were collected during 2019 from 33 countries in three regions:
- 225 isolates, Asia-Pacific (APAC);
- 790 isolates, Europe (EUR);
- 146 isolates, Latin America (LATAM).
- These E. coli isolates were tested by the CLSI broth microdilution method.
- 255 (22.0%) of these isolates exhibited the ESBL phenotype criteria of MICs >2 mg/L for at least 2 of the following antibiotics: aztreonam, ceftazidime, ceftriaxone, or cefepime.
- Whole genome sequencing (WGS) and in silico analysis were used to screen for resistance genes and to assess epidemiological types among the 255 ESBL-phenotype isolates. This isolate set included
- 116 MDR and 139 non-MDR phenotypes and
- 2 carbapenem-resistant isolates.
- WGS was performed using MiSeq (Illumina, San Diego, CA, USA). – High quality genomic DNA was extracted using KingFisher Cell and Tissue DNA kit (Thermo Scientific, Waltham, MA USA) in a robotic workstation KingFisher[™] Flex Magnetic Particle Processor (Thermo Scientific).
- Total genomic DNA constituted input material for library construction using the Nextera XT[™] library construction protocol and index kit (Illumina) and sequenced on a MiSeq Sequencer using MiSeq Reagent Kit v3 (600 cycle) with a target depth of coverage >30X.
- Each raw data set was quality assured, error corrected, and de novo assembled using SPAdes v. 3.11.1.

 Sequencing data was screened in silico for resistance genes, multilocus sequence types (MLST; https://github.com/tseemann /mlst), virulence genes (VirulenceFinder v3.1.0), OH types (v. 5.1.0), and ClermonType phylogenetic groups (v. 4.3.0) using an in-house proprietary bioinformatic pipeline.

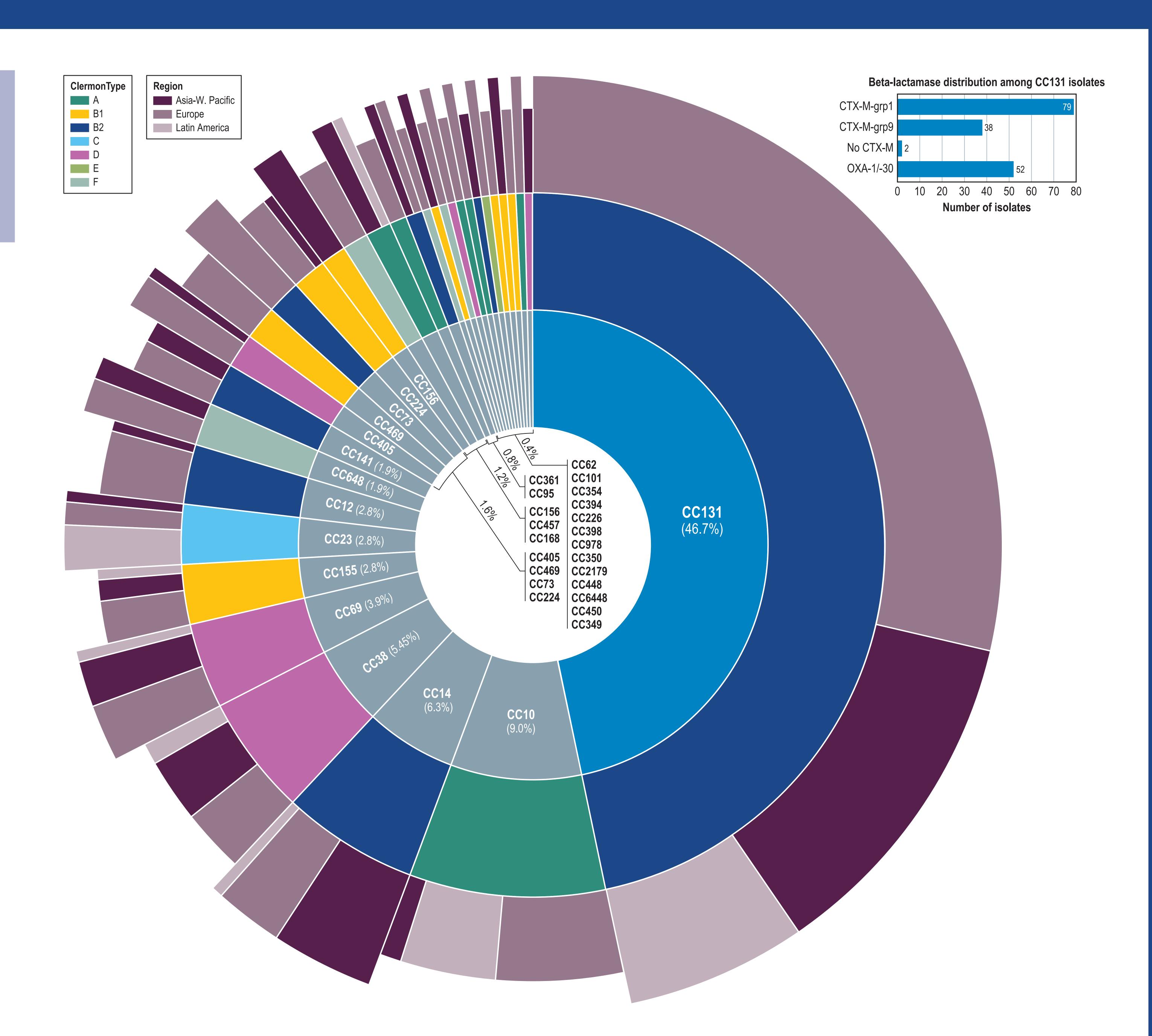
Results

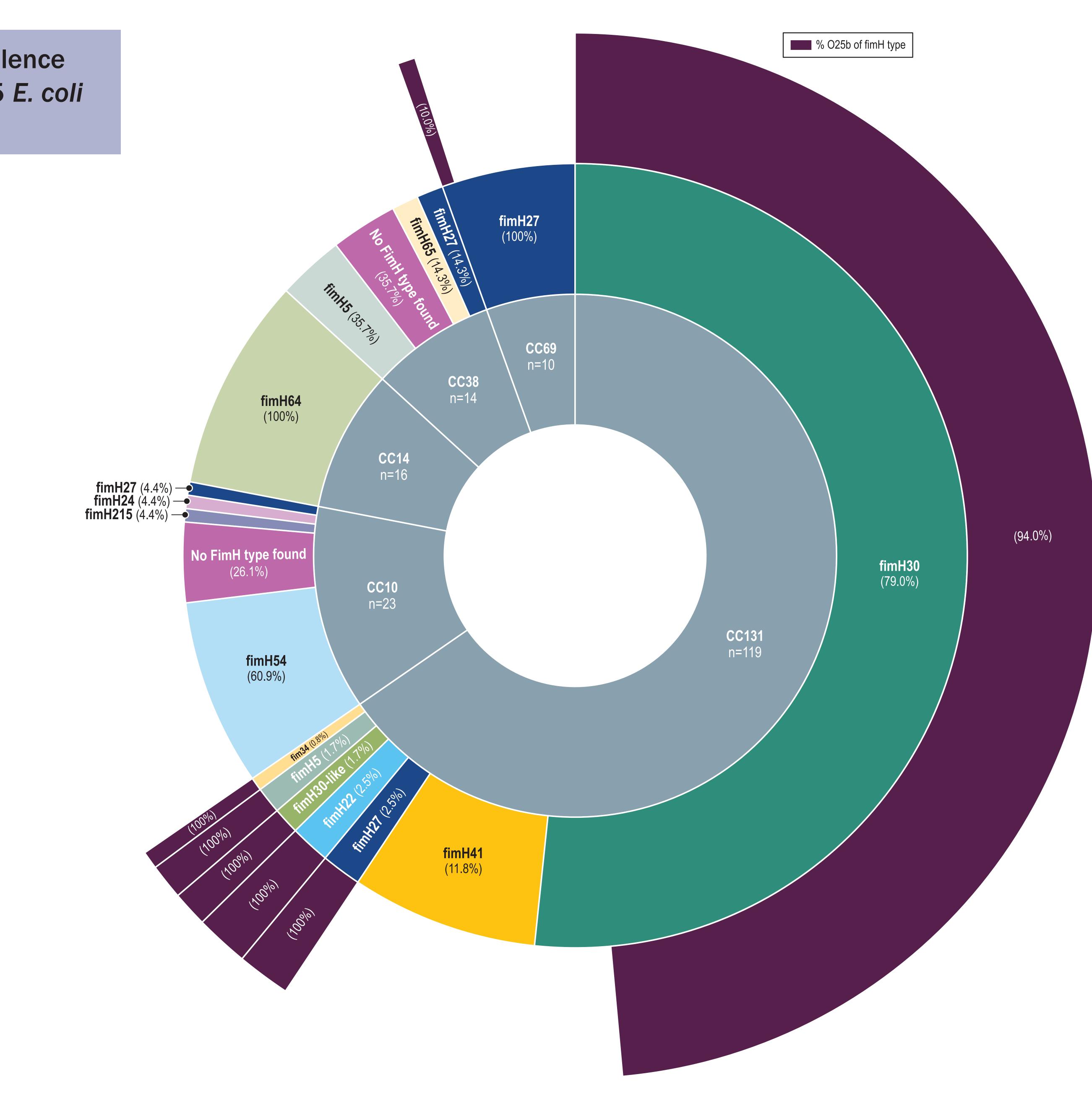
- CC131 (including 4 STs: ST131, ST2279, ST11258, and ST11259) was the most commonly identified CC overall, as it was seen in 119 of 255 isolates tested (46.7%) and across all three regions (APAC, 42.3%; EU, 49.0%; LATAM, 45.7%) (Figure 1).
- Other prevalent CCs were CC10 (23 isolates, 7 STs, 9 countries), CC14 (16 isolates, all ST1193, 11 countries), CC38 (14 isolates, 2 STs, 9 countries), and CC69 (10 isolates, all ST69, 7 countries).
- CC131 isolates were not detected in 8 countries: Brazil, the Czech Republic, Ireland, Malaysia, Panama, Romania, Sweden, and Taiwan.
- Based on ClermonTyping, 119 CC131 isolates belonged to phylogenetic group B2, 98 isolates belonged to serotype O25:H4, 96 isolates were associated with *fimH*30, and 14 isolates were associated with *fimH*41 (Figure 1).
- The *fimH* gene responsible for adhesion and possible invasive infection was detected in 237 of 255 (92.9%) isolates tested. – 33 distinct *FimH* types were detected.
- The most common *fimH* types were *fimH*30 (97 isolates, 6 STs, 25 countries), fimH27 (24 isolates, 8 STs, 13 countries), and fimH54 (21 isolates, 7 STs, 10 countries).
- FimH types were not identified in 18 isolates.
- Serotype 025b that elicits low IL-6 secretion and represents a high risk for progression to a febrile infection was detected in 102 isolates tested, 98 of which belonged to 025:H4 and CC131 (Figure 2).
- bla_{CTX-M-15} was the most common ESBL gene detected in 119 isolates (46.7%), followed by *bla*_{0XA-1/30} (60; 23.5%), *bla*_{CTX-M-27} (44; 17.3%), and $bla_{CTX-M-14}$ (24; 9.4%).
- $-bla_{0XA-1/30}$ was frequently detected with $bla_{CTX-M-15}$ (57 of 60 isolates).
- $-bla_{CMV}$ gene variants were detected in 17 isolates, only one of which belonged to CC131. - 2 carbapenem-resistant isolates carried either bla_{NDM-1} (Vietnam) or bla_{KPC-2} (Chile).
- 117 of 119 CC131 isolates carried either CTX-M-group 1 (79 isolates) or CTX-M-group 9 (38 isolates) encoding genes and 52 isolates carried OXA-1 encoding genes (Figure 1).

 Among the 255 isolates evaluated by WGS and analysis, 50 MLST types belonging to 32 CCs were observed.

Figure 1. Distribution of ST types among UTIcausing ExUS E. coli isolates in the SENTRY Program 2019

Figure 2. Distribution of virulence gene types among the top 5 E. coli clonal complex strains





Conclusions

- CC131 was the most predominant clonal complex among this geographically diverse ExUS set of EC isolates associated with
- These CC131 isolates were armed with virulence determinants and ESBL-encoding genes.
- Phylogenetic diversity was observed among the non-CC131 E. coli isolates causing UTIs.
- These data show that the prevalence of this high-risk clone in APAC, EUR, and LATAM remained lower than in the US, but other clones may be emerging, requiring continued surveillance.

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