NATIONAL CENTER FOR IMMUNIZATION AND RESPIRATORY DISEASES

Molecular Epidemiology of *Ureaplasma* Species Isolated from Neonates in the Global Multi-Center Child Health and Mortality Prevention Surveillance Network (CHAMPS)

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BACKGROUND

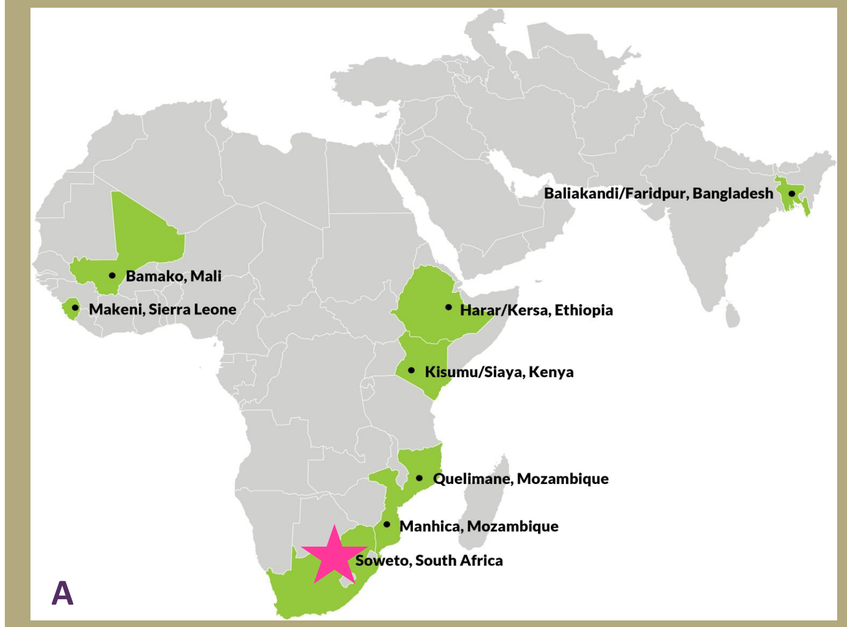
Ureaplasma species, including *U. urealyticum* and *U. parvum,* are infectious causes of stillbirth, neonatal sepsis, and preterm labor. Recent studies in South Asia and South Africa suggest *Ureaplasma* species are an underrecognized cause of neonatal infections in low- and middle-income countries. Diagnostic testing of neonatal clinical specimens for *Ureaplasma* is rarely done, and bacterial factors associated with birth complication and infection remain unclear.

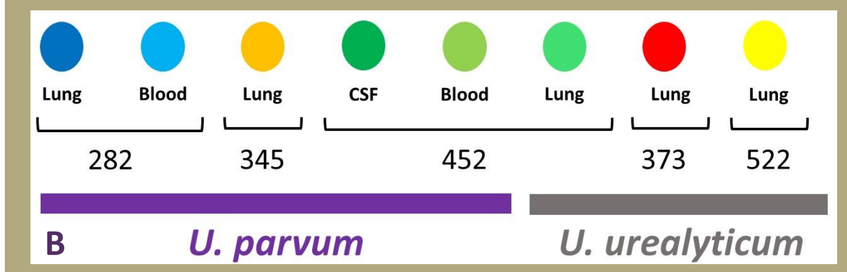
METHODS

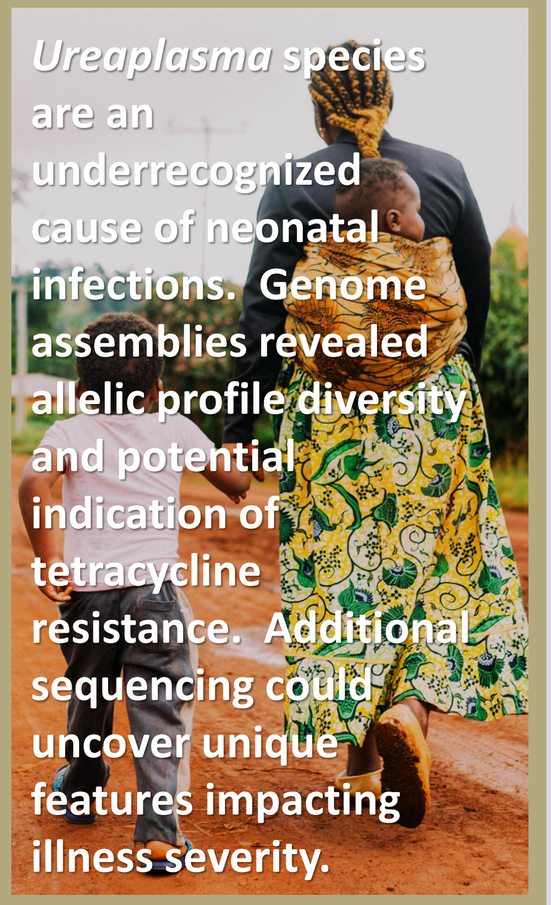
We performed additional testing on post-mortem blood, cerebrospinal fluid (CSF), and tissue specimens from Child Health and Mortality Prevention Surveillance (CHAMPS) cases in South Africa from May 2017 to January 2018. *Ureaplasma* species were initially detected by real-time reverse transcription polymerase chain reaction (RT-PCR) using custom TaqMan Array Cards. Specimens from CHAMPS cases in which *Ureaplasma* was detected in one or more specimen types were transferred to the Centers for Disease Control and Prevention (CDC) for culture, real-time PCR, and whole genome sequencing (WGS).

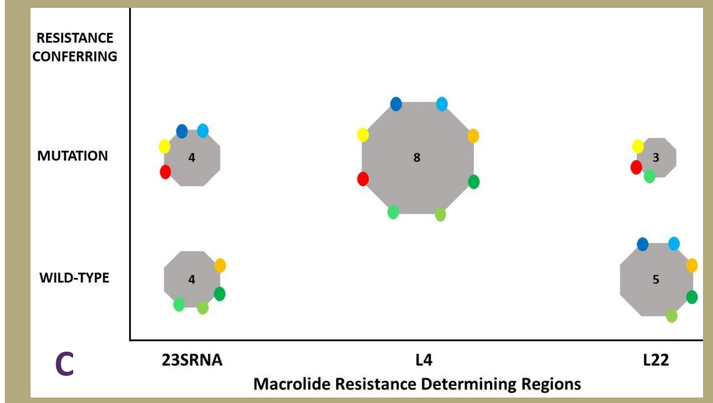
RESULTS

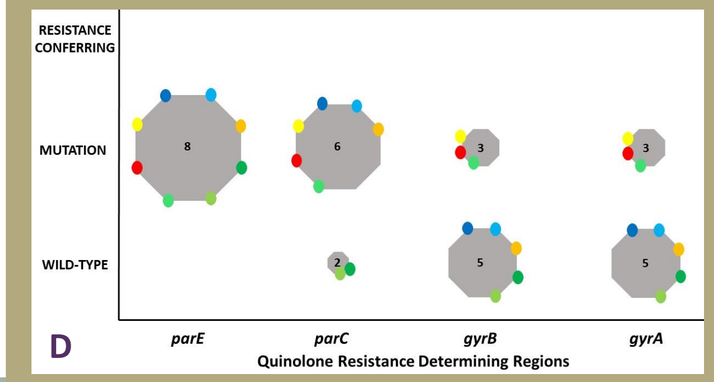
Ten isolates (5 *U. urealyticum*, 5 *U. parvum*) were recovered from 22 primary specimens, including lung tissue (n=5), blood (n=2), and CSF (n=3), from 6 cases where *Ureaplasma* was detected but not attributed to the cause of death. Genome assemblies were generated for 8 isolates and species identified by WGS matched real-time PCR species identification for all isolates. Expanded multi-locus sequence typing revealed diversity of isolates. Four (50%) isolates matched known sequence types (STs) which clustered in clonal complexes corresponding to species. Of these, 2 isolates from 2 different cases matched the same ST. Novel allelic profiles were identified in the remaining 4 (50%) isolates. Sequence evaluation for antimicrobial resistance revealed 1 isolate as tetracycline resistant through *tet (M)* gene acquisition. Analysis of additional specimens from cases enrolled at all CHAMPS sites is ongoing to further investigate the molecular epidemiology of *Ureaplasma* spp. and to identify relevant features that may contribute to poor clinical outcomes.

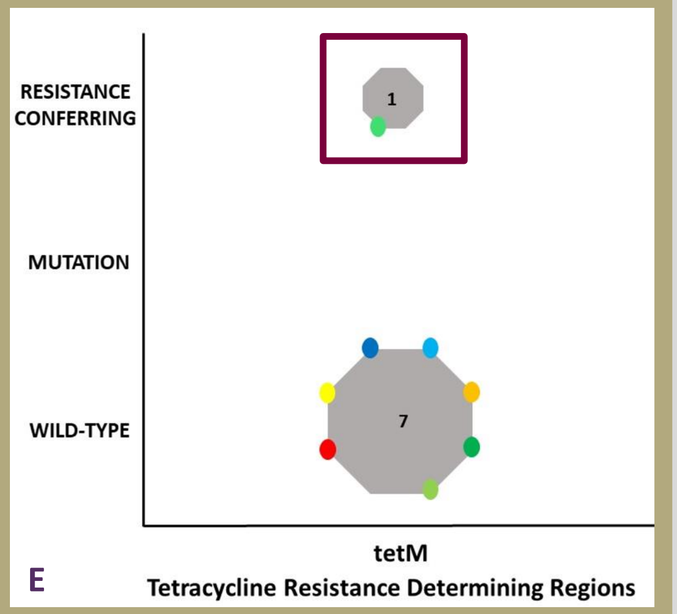






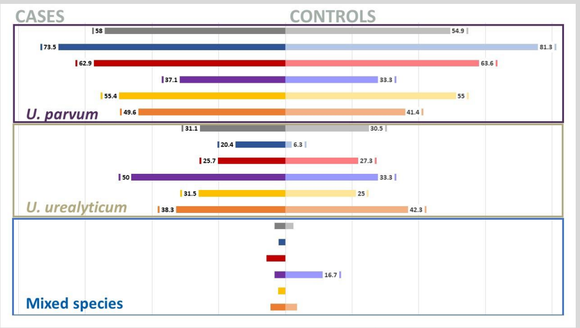




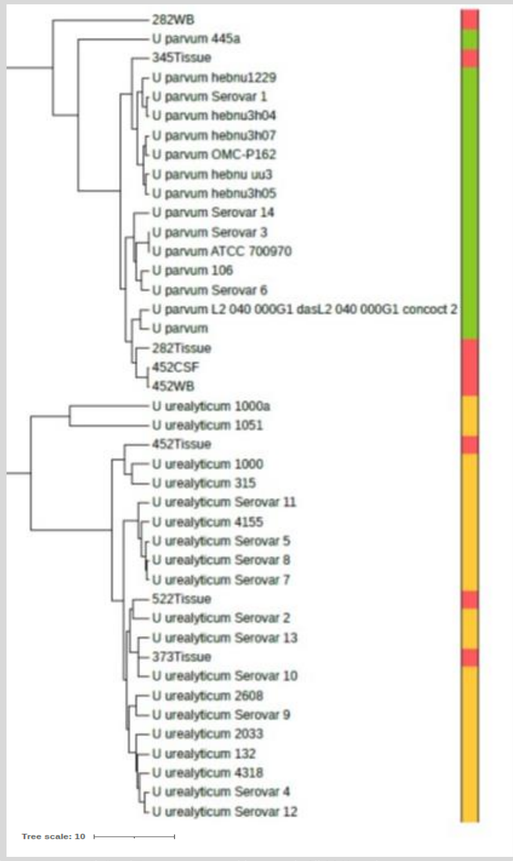


CHAMPS

GRAPHICS



Previous study investigating neonatal infections in South Asia (ANISA) revealed *Ureaplasma* as the leading attributable bacterial pathogen in the casual chain (Saha et al., Lancet). *Ureaplasma* species detections in NP/OP swabs at each study site separated by cases and controls. Data shown as a percentage for a given site (numeric percentage not displayed when < 5%). ALL SITES (gray) (n=402 cases, n=82 controls); Odisha, India (yellow) (n=98 cases, n=16 controls); Vellore, India (purple) (n=35 cases, n=11 controls); Sylhet, Bangladesh (orange) (n=115 cases, n=29 controls); Matiari, Pakistan (red) (n=62 cases, n=6 controls); Karachi, Pakistan (blue) (n=92 cases, n=20 controls).



Phylogenetic tree with 8 isolate genomic assemblies in red. All 14 *Ureaplasma* serovars spanning both species, *U. urealyticum* (orange) or *U. parvum* (green), are included.

Figure A: Map of 7 CHAMPS countries; star indicates site with specimens sequenced (South Africa)
Figure B: Real-time PCR (qPCR) and WGS *Ureaplasma* species determination for isolates from different clinical specimen types (whole blood, lung tissue, cerebral spinal fluid (CSF)); number indicates specimen identifier.
Figure C, D, E: Examining known macrolide (figure C), quinolone (figure D), and tetracycline (figure E) resistance determining regions from the WGS data for the 8 isolates; wild-type indicates no change from reference sequences (RFs); mutation indicates deviation from RFs with unknown evidence of resistance; resistance conferring indicates deviation from RFs with documented evidence of resistance. Number and shape size correspond to number of isolates represented.

CONTACT INFO

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