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NATIONAL CENTER FOR IMMUNIZATION AND RESPIRATORY DISEASES

Genomic characterization of *Klebsiella pneumoniae* isolates from deaths in children under 5 years of age identified through the CHAMPS network

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BACKGROUND

- *Klebsiella pneumoniae* (KP) is the predominant organism attributed to deaths at Child Health and Mortality Prevention Surveillance (CHAMPS) sites in sub-Saharan Africa and South Asia.
- Recent data indicate a rise in multidrug resistant and hypervirulent KP.
- We performed genomic characterization of KP isolates from CHAMPS cases to investigate diversity, virulence, and antimicrobial resistance (AMR) with the goal of informing development of vaccines and other therapeutics.

METHODS

- KP isolates cultured from post-mortem blood or cerebrospinal fluid (CSF) specimens from Mali (n=13), Kenya (n=38), Sierra Leone (n=39), Bangladesh (n=19) and Ethiopia (n=37) underwent whole genome sequencing (WGS) at International Centre for Diarrhoeal Diseases Research, Bangladesh (icddr,b) and Centers for Disease Control and Prevention, Atlanta (CDC).
- WGS data were analyzed by KP-specific genomic tools Kleborate (**GitHub - katholt/Kleborate**) and Pathogenwatch (**Pathogenwatch | A Global Platform for Genomic Surveillance**).

RESULTS

- Among 146 isolates identified as KP by various microbiological methods at CHAMPS site laboratories, 114 isolates were identified as KP by WGS **(Figure 1)**. Among these, **54 STs were identified, including novel types** in Sierra Leone (n=7), Mali (n=5) and Ethiopia (n=2).
- In total, 44 K-loci (capsular polysaccharide) and 7 O-loci (lipopolysaccharide) types were detected. **Diverse K-loci (10-18 unique types) were observed within each country. O1/O2v1 comprised the majority of isolates** in Kenya (50%), Sierra Leone (42%), Bangladesh (57%) and Ethiopia (44%) while O1/O2v2 was dominant in Mali (58%) **(Figure 2)**.
- Over 50% of strains from Sierra Leone, Bangladesh and Ethiopia possessed yersiniabactin siderophores, a virulence factor common among hospital-associated KP strains **(Table 1)**. **Extended-spectrum beta-lactamase genes were detected in 58-92% of KP isolates from each country** and a carbapenem resistance gene was identified in 57% of Bangladeshi isolates **(Figure 3)**.

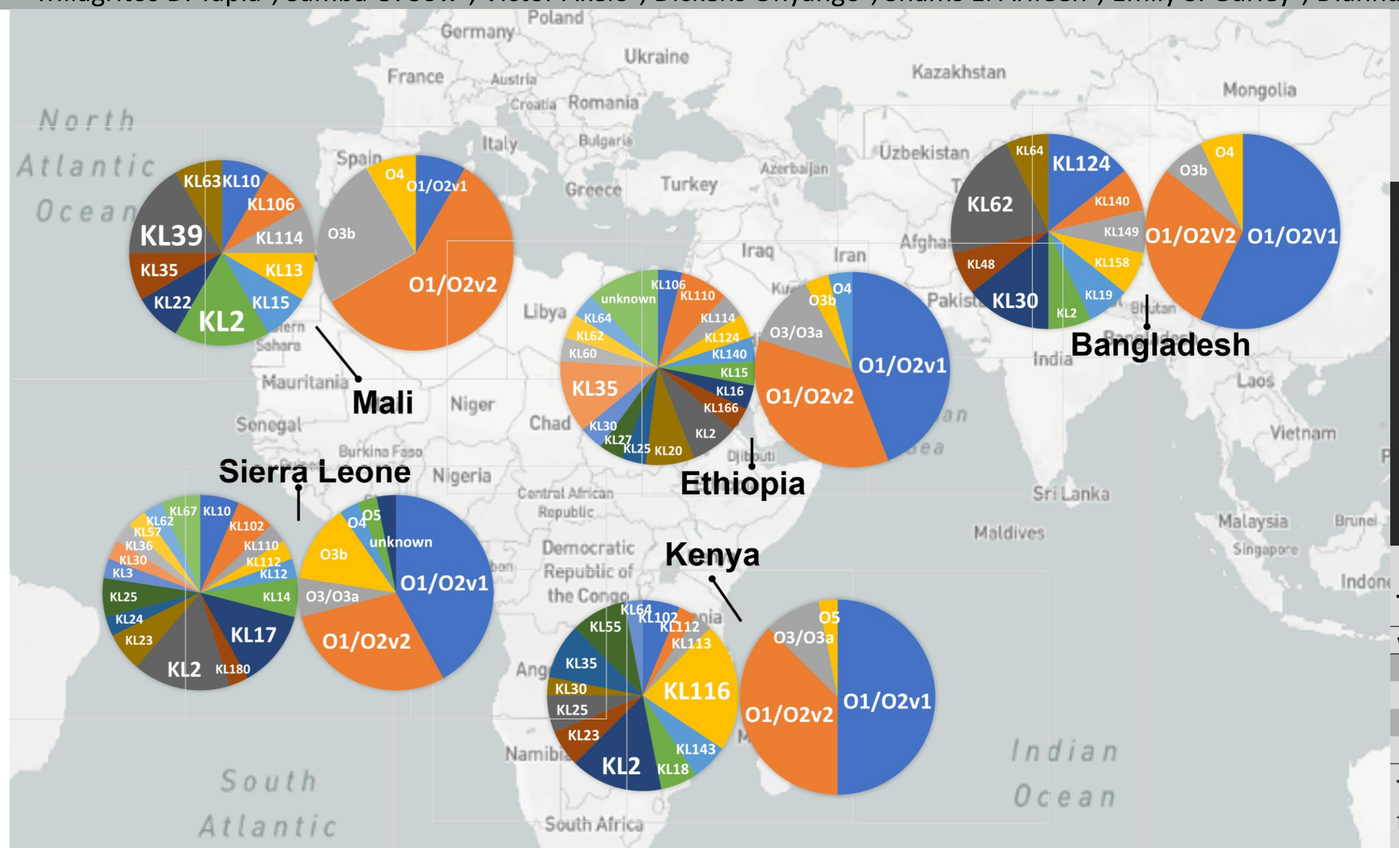

Figure 2. Distribution of K (capsular polysaccharide; left pie) and O (lipopolysaccharide ;right pie) locus in KP isolates by country.

Hypervirulence and AMR are common among *Klebsiella pneumoniae* isolates associated with child deaths in low-and-middle-income countries. Ongoing surveillance utilizing genomics tools is crucial for the development of vaccines and antimicrobial treatments.

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FIGURES

Figure 1. Number of *Klebsiella pneumoniae* (KP) and other *Klebsiella* spp. genomes from CHAMPS participate countries

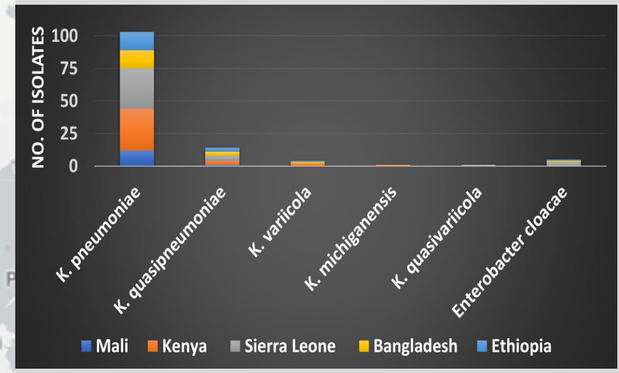
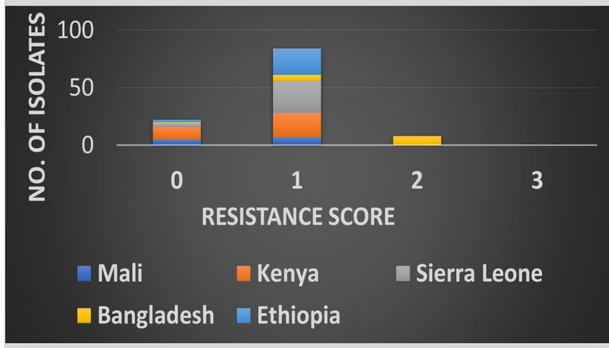


Table 1. Virulence score in KP isolates by countries.

Virulence Score	Mali	Kenya	Sierra Leone	Bangladesh	Ethiopia
0	8 (67%)	21 (66%)	13 (42%)	5 (36%)	12 (48%)
1	4 (33%)	11 (34%)	18 (58%)	9 (64%)	13 (52%)
2-5	0	0	0	0	0
Total	12 (100%)	32 (100%)	31 (100%)	14(100%)	25 (100%

The virulence score ranges from 0 to 5: 0 = negative for all of yersiniabactin (ybt), colibactin (clb), aerobactin (iuc); 1 = ybt only; 2 = ybt and clb (or clb only); 3 = iuc (without ybt or clb); 4 = iuc with ybt (without clb); 5 = ybt, clb and iuc

Figure 3. AMR score in KP isolates by countries



The resistance score ranges from 0 to 3:
0 = no ESBL(extended-spectrum beta-lactamases), no carbapenemase;
1 = ESBL, no carbapenemase;
2 = Carbapenemase without colistin resistance;
3 = Carbapenemase with colistin resistance

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