Epidemiology and natural history of ESBL-producing and carbapenem-resistant Enterobacteriaceae rectal colonization among organ transplant recipients

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Background: We prospectively investigated the natural history of ESBL-Enterobacteriaceae (ESBL-E) and CRE rectal-colonization among solid organ transplant (SOT) recipients at the University of Pittsburgh Medical Center (UPMC).

Material/methods: Patients undergoing SOT from 8/2015-10/2016 were consented. Peri-rectal swabs were collected each week until 90 days post-SOT, and cultured using CHROMagar plates. Patients were followed for 6 months after SOT.

Results: 191 transplanted patients were enrolled: 87 lungs, 73 liver, 19 kidneys, 7 heart, 4 small bowel, and 1 pancreas. Median age was 58 years. 88% were white. Median time from SOT to first swab was 3 days, and median of 3 swabs/patient were collected. 21% (38) were rectal-colonized: 15 with CRE (K. pneumoniae most common), and 28 ESBL (E. coli most common); 5 patients were rectal-colonized with both CRE and ESBL-E. One patient was rectal-colonized with 2 CRE. All CR-K. pneumoniae and K. oxytoca were KPC-producers. Rectal-colonization rates among lung, liver and SB were 23%, 23% and 25% versus 0% among heart and kidney patients. 31% were detected in the first swab. In other pts, median time from SOT to rectal-colonization was 22 d. 76% of pts had persistent rectal-colonization (≥2 swabs +). 36% and 15% of liver and lung transplant patients with rectal-colonization developed disease: 3 intra-abdominal infection, 3 pneumonia/empyema, 3 urinary tract infection and 1 wound; 2 patients had bacteremia. 21% (8/38) of rectal-colonized patients developed disease vs. 1% (2/151) of non-rectal-colonized (p<0.0001). Rectal-colonization was the only significant
risk factor for disease. 20% of pts with disease died; hospitalization stay was significantly prolonged in survivors (median: 75 d). We performed WGS on 18 ST258 *K. pneumoniae* isolates from rectal and other sites (this study), as well as other isolates from UPMC and elsewhere in the US (prior to this study). Present study isolates clustered tightly together, forming a novel sublineage that was distinct from other clade II isolates from UPMC and elsewhere. Isolates within this new sublineage differed on average by 17 SNPs, and differed from other clade II and clade I isolates by an average of 85 and 240 SNPs, respectively. Six of 13 lung transplant patients within a 60-day period were rectal-colonized with KPC-*K. pneumoniae*, yielding a transmission rate of 46%. WGS revealed 2-6 SNP differences between their isolates.

**Conclusions:** Rectal-colonization with CRE or ESBL-E was common among lung and liver patients, and a risk factor for subsequent disease. Patients developed disease due to rectal-colonization isolates. 67% of rectal-colonized patients were colonized ≥ 2 weeks post-SOT. WGS revealed cryptic nosocomial acquisition of rectal-colonized ST258 KPC-Kp, which later caused disease. Rectal screening and infection prevention measures are merited among lung and liver transplant recipients.