Background

Extra-intestinal pathogenic Escherichia coli (ExPEC) carry a broad range of virulence factors (VFs) that are associated with site-specific disease. ExPEC VF detection is leading cause of bacteraemia and are associated with urinary tract, intra-abdominal/hepatobiliary, respiratory tract and skin/soft tissue infections, amongst others. In severely immunocompromised patients with neutropenia, E. coli bacteraemia frequently occurs in the absence of any clinically-identifiable focus as a consequence of translocation from the gut. The contribution of ExPEC VFs in this context is undefined. We hypothesised that, in the setting of neutropenia with no identifiable infective focus, ExPEC strains with fewer VFs would be able to translocate across the gut and survive hematogenously compared with isolates from immunocompetent patients. In addition, we posited that E. coli bacteraemia might be polyclonal in patients with neutropenia.

Aims & Methods

Study aims were as follows:

1. To compare ExPEC VF gene profiles of bacteraemia isolates from immunocompetent vs. neutropenic patients (where the focus of infection is likely translocation from the gut).

2. To establish whether E. coli bacteraemia is polyclonal or monoclonal amongst isolates from immunocompetent vs. neutropenic patients.

Immunocompetent and neutropenic adults with E. coli bacteraemia were recruited prospectively (Figure 1) and the source of bacteraemia determined (UK REC approval ref: 15/NE/0087). Random amplified polymorphic DNA (RAPD) fingerprinting was utilised to assess clonality of E. coli bacteraemia. ExPEC VF gene (31 in total) profiles were established in silico following whole genome sequencing (WGS) using SRST2 with standard parameters in conjunction with the VF database. Total number and individual VF gene distributions were compared across isolates associated with site-specific disease.

Results

Fifty (50) bacteraemia isolates from 49 immunocompetent patients and 8 isolates from 8 neutropenic patients were available for comparative VF gene analysis. RAPD excluded the possibility of polyclonal bacteraemia (Figure 2) prior to WGS of isolates. Thirty (30) multi-focus sequence types (STs) were identified, the most common being STs 131, 73, 69, 127 and 12 (Figure 3). Total number of VF genes (Figure 4) and the distribution of individual VF genes (Figure 5) varied significantly between isolates from immunocompetent (urinary vs. non-urinary focus) vs. neutropenic patients.

Discussion

E. coli bacteraemia strains originating from urinary tract infective foci harboured significantly more ExPEC-associated VF genes than strains originating from both non-urinary tract foci and neutropenic patients with unknown foci of infection (presumed gut translocation source).

The observation that isolates originating from immunocompetent patients from non-urinary tract infective foci were not significantly dissimilar to isolates from neutropenic patients with unknown foci of infection suggests they likely originated from a common location, i.e. the gastrointestinal tract.

This study has revealed the diversity of E. coli strains associated with both history of recurrent UTI/presence of a urinary catheter (OR 12.82, 95% CI 1.24-136.65, p=0.032) and total number of virulence factor genes (OR 1.21, 95% CI 1.01-1.46, p=0.039) with independent predictors of urinary vs. non-urinary focus of infection amongst immunocompetent patients in a model inclusive of age, gender, Charcot-morbilloid index, antibiotic use within the 28 day period prior to the blood culture being taken, and history of recurrent UTI/vaginal catheter.