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Molecular epidemiology and clinical outcomes of Clostridium difficile infections from North West London hospitals: is 220 an under-appreciated severe ribotype?

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Background: Despite year on year reductions in the number of *Clostridium difficile* infection (CDI), management of CDI remains a challenge in the UK and internationally**.** Certain *C. difficile* ribotypes have been associated with complex disease phenotypes including recurrence and/or increased severity however data related to currently prevalent ribotypes are limited.

Material/methods: From August 2011 to June 2013 all stool samples from symptomatic patients submitted for *C. difficile* testing that were positive for GDH (Glutamate dehydrogenase) and C. difficile PCR were cultured. PCR ribotyping was performed on all isolates. Routine clinical and demographic data was retrieved and linked to samples.

Results: A total of 758 *C. difficile* isolates were ribotyped from 715 different patients (aged over 2 years). The median age was 74 (60-83) and 54% were female. Eighty-six separate ribotypes were identified. Ribotypes 002 and 015 were the most common, accounting for over 20% of all ribotypes. There were only 5 isolates (0.66%) of ribotype 027. Most isolates underwent testing for toxin production by ELISA: 39% of these tested positive.

93 patients (13%) died within 30 days of *C. difficile* isolation. Of isolates that tested positive for toxin production, 30/198 (15.15%) died within 30 days; only 31/283 (10.95%) of toxin negative patients died within 30 days (p= 0.21). Ribotype 220 was associated with overall reduced survival.

Inflammation measurements were assessed as markers of severity: comparison of all ribotypes with ribotype 220 demonstrated significant differences in CRP ($p<0.05$), creatinine ($p<0.05$), and albumin

($p<0.05$) but not leukocyte count ($p=0.1$). Ribotype 220 isolates also were more likely to be associated with toxin production.

Conclusions: A wide range of C. difficile ribotypes are responsible for CDI presentations; ribotype 027 is now rare. Ongoing surveillance is required for novel lineages that may be associated with more severe disease. Further investigation of such lineages will require genomic analyses that are ongoing.