EP0276
ePoster Session
Travel medicine and international health

A cross-sectional multi-centre study on Clostridium difficile infections in representative regions of Germany, Ghana, Tanzania, and Indonesia

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Background: *Clostridium difficile* infections (CDI) have become an emerging health threat usually ranging from diarrhea to pseudomembranous colitis which can end up in toxic megacolon with high mortality. Since antibiotics have been identified as a major risk factor, we postulate that prevalence rates of CDI and the distribution of *C. difficile* strains differ between geographical regions depending on the regional use of antibiotics.

Material/methods: A cross-sectional, multi-centre study was performed in representative communities in Germany, Ghana, Tanzania and Indonesia. Patients with diarrhea and asymptomatic control individuals of different ages were screened for the presence of *C difficile* in stool samples. Cultured *C. difficile* strains were further characterized using PCR ribotyping, MALDI-TOF MS, genome analysis, determination of toxin genes and toxin production, as well as antibiotic susceptibility testing. Potential risk factors were determined using a standardized questionnaire.

Results: A total of 1,201 stool samples from 608 patients and 594 healthy control individuals were included. Prevalence rates of CDI ranged from 5% in Africa to 15% and 27% in diarrhoeal patients from Indonesia and Germany, respectively. Nontoxigenic strains of ribotype 084 were most abundant in Africa. In contrast, toxin A+/B+ ribotypes 001/072 and 078 predominated in Germany. In Indonesia, most strains belonged to toxin A-/B+ ribotype 017. Depending on geographical origin, major

differences for mobile genetic elements were seen. All isolates were susceptible to vancomycin and metronidazole, respectively. Mirroring the antibiotic use, however, moxifloxacin resistance was absent in African *C. difficile* isolates but present in Indonesian (24%) and German ones (67%).

Conclusions: CDI is a global health threat with geographically different prevalence rates that might reflect distinct use of antibiotics. Significant differences for distributions of mobile genetic elements, ribotypes, toxin production, and antibiotic susceptibilities were observed. If diagnosis relies only on detection of toxin A from stool samples, several CDI cases especially originating from Africa or Asia might be left undetected. This work was funded by the Federal State of Lower Saxony, Niedersächsisches Vorab (VWZN2889).