

**Risk factors for acquisition and characterization of extended-spectrum beta-lactamase-producing Enterobacteriaceae in healthy travellers**

M. Vading<sup>1</sup>, P. Nauc ler<sup>2</sup>, S. Wiklund<sup>3</sup>, A. Iversen<sup>1</sup>, M. Kalin<sup>2</sup>, C. Giske<sup>1</sup>

<sup>1</sup>MTC - Karolinska Institutet- Karolinska University Hospital, Stockholm, Sweden

<sup>2</sup>Karolinska university hospital- dep of infectious diseases, Stockholm, Sweden

<sup>3</sup>Department of Medicine- Solna, Unit of Infectious Diseases, Karolinska Institutet, Stockholm, Sweden

**Objectives**

The objective of this study was to investigate fecal carriage and bacterial characteristics of ESBL-producing Enterobacteriaceae (EPE) after traveling to endemic areas.

**Methods**

Travelers to four regions with an estimated high prevalence of EPE: the Indian subcontinent, Southeast Asia, northern Africa and the Middle East, were asked to participate in the study by a vaccination clinic in Stockholm. Participants sent in one fecal sample before traveling and one upon return. Samples were plated on selective agar (ChromID ESBL, bioMerieux, France), followed by species determination (MALDI-TOF, Bruker, Germany), susceptibility testing with the EUCAST disk diffusion method and ESBL confirmation tests (Rosco, Denmark). ESBL-genotyping was done with Check-MDR (Check-Points, The Netherlands), and epidemiological typing with DiversiLab (bioMerieux). Real-time PCR was used for screening of resistance genes, phylogrouping of ESBL-producing *Escherichia coli*, and screening of *E. coli* virulence factors. Data regarding background information about the participants and the trip was collected from two questionnaires.

**Results**

Between May 2013-September 2014 168 travelers completed the study. Eleven travelers (6.5%) were excluded due to pretravel EPE colonization leaving 157 participants. Upon return, 49/157 (31.2 %) were colonized by EPE. Colonization was seen in 12/64 (18.8%) traveling to Southeast Asia, 24/52 (46.2%) to India, 11/23 (47.8%) to Northern Africa and 2/18 (11.1%) to the Middle East. Laboratory tests are ongoing and so far completed in 38 of the travelers, where 46 different strains were found.

The median travel time was 14 days both for travelers testing positive and negative for EPE. Diarrhea during the trip was significantly more common among the EPE positive participants, 19/49 (38.8%), compared to 22/108 (20.4%) in the negative group (P=0.02). Contact with healthcare facilities and antimicrobial treatment during the trip was also significantly higher in the EPE-positive group in univariate analysis (P=0.005 and 0.035 respectively). Multivariable analysis is ongoing.

Detected EPE isolates were *E. coli* (n=44), *Klebsiella pneumoniae* (n=1) and *Citrobacter freundii* (n=1). *E. coli* isolates belonged to phylogroup A (n=19), B1 (n=9), B2 (n=3) and D (n=3). CTX-M-1-group was most common (n=32) followed by CTX-M-9-group (n=9). All strains were resistant to cefotaxime. Co-resistance was distributed as follows: piperacillin-tazobactam 11, gentamicin 23, amikacin 2, ciprofloxacin 5 and trimethoprim-sulfamethoxazole 28 isolates. Genes encoding aminoglycoside or quinolone resistance were seen in 22 isolates. Apart from fimH, found in 34 isolates, only 10 isolates carried any of the virulence factors.

**Conclusion**

The risk of intestinal colonization with EPE is significant when traveling to India and northern Africa and elevated also when traveling to Southeast Asia or the Middle East. EPE found in this study differ in phylogroups and carry less virulence factors compared to uropathogenic strains. Diarrhea during travel and antimicrobial treatment are risk factors for fecal EPE colonization.