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Letter to the Editor

Intestinal colonisation with multidrug-resistant Enterobacteriaceae: Screening of Swiss military deployed to Kosovo

Sir,

International travel is a known risk factor for intestinal colonisation with extended-spectrum cephalosporin-resistant (ESC-R) Enterobacteriaceae [1], thereby contributing to their spread from high- to low-endemicity countries such as Switzerland. This phenomenon is also observed in military personnel stationed in high-endemicity areas. For instance, French soldiers deployed to Afghanistan and Côte d'Ivoire showed colonisation rates with ESC-R *Escherichia coli* of >50% [2]. In Switzerland, military personnel have been deployed for peacekeeping missions to various regions for decades.

In this study, the extent of intestinal colonisation with ESC-R- and/or colistin-resistant (COL-R) Enterobacteriaceae in military staff deployed to Kosovo from November 2017 to April 2018 was analysed. Stools were collected before and after the service (within 1 week). As done previously, samples were enriched overnight in Luria–Bertani broth containing cefuroxime (3 mg/L) or colistin (2 mg/L). From each tube, aliquots were plated on ChromID® ESBL/Carba (bioMérieux) or CHROMagar™ Orientation plus colistin (4 mg/L) and vancomycin (8 mg/L), respectively, and were incubated overnight [3]. At least five colonies were selected from each positive agar plate for further analyses. Species identification was achieved by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF/MS) (Bruker). Minimum inhibitory concentrations (MICs) for antibiotics were determined using Sensititre™ GNX2F microdilution plates and were interpreted according to 2019 European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria (www.eucast.org). Whole-genome sequencing was performed on a NovaSeq 6000 System (Illumina Inc.) and reads were analysed using tools from the Center for Genomic Epidemiology (www.genomicepidemiology.org/) [1,3].

Both pre- and post-deployment stools were available for 21 participants. As shown in Table 1, two subjects were already colonised with COL-R *E. coli* isolates before going to Kosovo: one isolate carried the *mcr-1.2* gene in a 33-kb IncX4 plasmid that is frequently reported worldwide (data not shown) [3], while the other isolate showed amino acid substitutions in the chromosomal PmrAB two-component system. Upon return to Switzerland, three (14.3%) deployed persons (including one previously colonised with the *mcr-1.2*-positive strain) screened positive for ESC-R *E. coli.* Such strains were of different sequence types (ST2540, ST69 and ST484) not belonging to hyperepidemic lineages, and all carried the $bla_{CTX\text{-}M\text{-}15}$ gene along with other antimicrobial resistance genes (Supplementary File S1). Strains with reduced susceptibility to colistin, carbapenems and/or fluoroquinolones were not detected (Table 1).

The prevalence of gut colonisation with ESC-R Enterobacteriaceae recorded in the present study (14.3%) was similar to that found in a study involving German soldiers deployed internationally between 2007–2015 (4.7%) and among French soldiers sent to French Guiana during 2012 (5.3%) [2,4]. However, it was considerably lower than the incidence among French army persons returning from Côte d'Ivoire and Afghanistan (49% and 88%, respectively) in 2012 [2].

Based on the current results, we speculate that the recorded colonisation rates in soldiers returning to their home countries do not fully mirror the prevalence of antimicrobial resistance in the region of deployment. Unfortunately, data on colonisation rates with ESC-R *E. coli* in the local population in Kosovo are not available. However, in 2017 the surrounding regions in Eastern and South Eastern Europe showed up to 40% of *E. coli* from clinical samples to be ESC-R (https://ecdc.europa.eu/en/publications-data/surveillance-antimicrobial-resistance-europe-2017). This is much higher than the 10% found in Switzerland during the same time period (www.anresis.ch). Therefore, colonisation rates in military personnel returning from Kosovo could have been predicted to be much higher than the 14% actually found in the participants in the current study.

This unexpected low colonisation rate in Swiss military personnel could have several reasons. It is possible that Kosovo has overall lower resistance rates than neighbouring countries. More likely, the low rates found in these subjects could be due to their different hygiene conditions compared with the local population, thus preventing them from acquiring multidrug-resistant bacteria from food chain, animals and/or the environment. Looking at the participants in this study, we note for instance that approximately one-half of them ate >50% of their meals inside the military compound (Table 1). This behaviour is very different to what is observed in travellers visiting tropical and subtropical countries who show considerably higher rates of gut colonisation owing to their closer contact and more frequent interaction with the local human and non-human settings [1].

These data indicate that deployment-related colonisation rates with ESC-R *E. coli* are slightly higher than those recorded in the healthy population in Switzerland (~7%) [5] but are considerably lower than those observed in international travellers (up to 75%) [1]. Therefore, the impact of military personnel returning from international deployment on the spread of antimicrobial resistance is probably less important than that of travellers. Nevertheless, larger studies assessing military personnel returning from different countries are required to properly assess the impact of these subjects on the worldwide spread of antimicrobial resistance.

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Table 1
Demographic data of participants, colonisation status before and after travelling, and phenotypic and molecular characteristics of recovered isolates.

ID	Age (years)	Sex	Phenotypic and molecular characteristics of ESC-R and/or COL-R strains (if any)[a]		Potential risk factors during deployment			
			Stools collected before deployment	Stools collected after deployment	Antibiotic use	Hospitalisation	Diarrhoea	Food outside military compound (times/week)
ID6	24	M	Negative	Negative	No	No	No	7
ID10	26	M	Negative	Negative	No	No	Yes	6
ID12	27	M	Negative	Negative	No	No	Yes	1
ID13	31	M	Negative	Negative	No	No	Yes	1
ID22	47	M	Negative	Negative	N/A	N/A	N/A	N/A
ID25	25	F	*E. coli*: COL (4), CTX (≤1), FEP (≤2), MEM (≤1), CIP (1), GEN (≤1), DOX (8), SXT (4) ST69-like; *mcr-1.2*, bla_{TEM-1B}, *aph(3″)-Ib*, *aph(6)-Id*, *aadA1*, *aadA2*, *mdf(A)*, *cmlA1*, *sul2*, *sul3*, *tet(A)*, *dfrA5*, GyrA (S83 L), ParC (S80R), [PmrB: H2R, S138 N, D283 G]; Col440II, FIB, FII, Q1, X1, X4	*E. coli*: COL (≤0.25), CTX (16), FEP (≤2), MEM (≤1), CIP (≤0.25), GEN (≤1), DOX (4), SXT (1) ST2540; $bla_{CTX-M-15}$, *aadA5*, *mdf(A)*, *tet(A)*, *dfrA17*, [PmrB: D283 G, Y358 N]; FIA, FIB, HI1A, HI1B	N/A	N/A	N/A	N/A
ID26	25	F	Negative	Negative	N/A	N/A	N/A	N/A
ID29	49	F	Negative	*E. coli*: COL (≤0.25), CTX (16), FEP (≤2), MEM (≤1), CIP (≤0.25), GEN (≤1), DOX (≤2), SXT (≤0.5) ST69; $bla_{CTX-M-15}$, *qnrS1*, *mdf(A)*, [PmrB: H2R, S138 N, D283 G]; FII, X4	No	No	Yes	3
ID30	29	F	Negative	Negative	No	No	Yes	7
ID31	33	F	Negative	Negative	Yes	No	No	7
ID34	27	M	Negative	Negative	No	No	Yes	1
ID37	32	M	Negative	Negative	No	No	No	0
ID38	31	F	Negative	Negative	No	No	Yes	1
ID39	30	F	Negative	*E. coli*: COL (≤0.25), CTX (32), FEP (≤2), MEM (≤1), CIP (≤0.25), GEN (≤1), DOX (≤2), SXT (≤0.5) ST484; $bla_{CTX-M-15}$, *qnrS1*, *mdf(A)*; FIC	No	No	No	7
ID40	29	F	Negative	Negative	Yes	No	1	N/A
ID42	28	F	*E. coli*: COL (>4), CTX (≤1), FEP (≤2), MEM (≤1), CIP (≤0.25), GEN (≤1), DOX (≤2), SXT (≤0.5) ST420-like; *mdf(A)*, [PmrA: T31S, I128 N, G144S; PmrB: H2R, E123D, T156 K, D283 G, V351I]; Col156, FIB, FII	Negative	No	No	Yes	1
ID64	26	M	Negative	Negative	N/A	N/A	N/A	N/A
ID65	25	M	Negative	Negative	No	No	Yes	3
ID66	23	M	Negative	Negative	No	No	No	1
ID69	29	M	Negative	Negative	No	No	1	0
ID70	28	M	Negative	Negative	No	No	No	4

ESC-R, extended-spectrum cephalosporin-resistant; COL-R, colistin-resistant; N/A, not available; COL, colistin; CTX, cefotaxime; FEP, cefepime; MEM, meropenem; CIP, ciprofloxacin; GEN, gentamicin; DOX, doxycycline; SXT, trimethoprim/sulfamethoxazole; MIC, minimum inhibitory concentration.

[a] Showing the following characteristics: bacterial species with antimicrobial phenotype (MIC in mg/L); sequence type (ST); antimicrobial resistance genes; and plasmid replicon types detected by whole-genome sequencing and implementing the Center for Genomic Epidemiology (CGE) analysis. Among the unknown mutations (according to the CGE analysis), only those for *pmrA* and *pmrB* have been reported in square brackets (as amino acid substitutions).

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Competing interests

None declared.

Ethical approval

Ethical approval was obtained from the local ethics committee [Ethikkommission Nordwest- und Zentralschweiz; BASEC 2017-01161].

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jgar.2019.08.027.

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