Rapid communication

Emergence of carbapenem-resistant ST131 Escherichia coli carrying bla\textsubscript{OXA-244} in Germany, 2019 to 2020

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The dissemination of carbapenem-producing Gram-negative bacteria is a major public health concern. We report the first detection of OXA-244-producing ST131 O16:H5 Escherichia coli in three patients from two tertiary hospitals in the south-west of Germany. OXA-244 is emerging in Europe. Because of detection challenges, OXA-244-producing \textit{E. coli} may be under-reported. The emergence of carbapenem resistance in a globally circulating high-risk clone, such as ST131 \textit{E. coli} is of clinical relevance and should be monitored closely.

\textit{Escherichia coli} of the ST131 lineage is considered as a successful and emerging high-risk pandemic multidrug-resistant \textit{E. coli} strain [1,2]. Typically, most ST131 \textit{E. coli} are resistant to third-generation cephalosporins but remain susceptible to carbapenems [3]. We detected three OXA-244-producing ST131 \textit{E. coli} from patient samples in two tertiary hospitals in the south-west of Germany between January 2019 and June 2020.

OXA-244 is a single-point mutation variant (Arg214Gly) of the globally circulating OXA-48 [3], resulting in lower minimum inhibitory concentration (MIC) values, which poses a major challenge for its detection [4,5].

The aim of our study was to investigate the genetic diversity of the emerging OXA-244-producing \textit{E. coli} in the Rhine-Neckar region using whole-genome sequencing.

Local surveillance measures for multidrug-resistant organisms

Since January 2019, the University Hospitals in Heidelberg and Mannheim, located in the south-west of Germany (Rhine-Neckar region), have implemented routine molecular typing by whole-genome sequencing (WGS) of non-repetitive multidrug-resistant Gram-negative bacteria (MDR-GN) from admission screening and clinical samples as part of the local infection control measures. Admission rectal screening for MDR-GN was performed for all risk patients, which includes (i) admission to intermediate and intensive care units, (ii) previous colonisation with multidrug-resistant organisms (MDRO) or contact with MDRO patients, (iii) contact with a high-prevalence setting or endemic region for MDRO (including travel and migration), (iv) chronic wounds and (v) close contact to animals, as previously described [6]. The cultural detection methods used a selective medium (ChromID ESBL, Biomérieux, Nürtingen, Germany) and were confirmed by antibiotic susceptibility testing (AST) with VITEK2 (Biomérieux) interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints v10.0 [7]. Carbapenemase genes were detected with an in-house PCR (data not shown) of all isolates with phenotypic resistance to carbapenem or with suspected carbapenem resistance (i.e. elevated MIC for carbapenems).

Only the first detected isolate from each patient was sequenced. Molecular characterisation was performed by short-read WGS using the Nextera DNA Flex Library Prep Kit (Illumina, San Diego, United States) and the MiSeq instrument (2 x 300 bp), as described previously [6]. Assembly was performed with Spades 3.13.0 [8]. Core genome was calculated using Roary [9] after annotation with Prokka 1.14.1 [10]. Coverage for each contig was extracted from the Spades output. Resistance genes were annotated using Abricate 1.0.0 with the database form the National Center for Biotechnology Information (NCBI) [11], the comprehensive antibiotic resistance database CARD [12], Antibiotic resistance gene-ANNOTation (ARG-ANNOT) [13] and Resfinder 3.0 [14] (latest update on 10 June 2020). Subtyping of the serotype and \textit{fimH} was performed using SerotypeFinder 2.0 (https://cge.cbs.dtu.dk/services/SerotypeFinder/) and FimTyper 1.0 (https://cge.cbs.dtu.dk/services/FimTyper/). Assembled draft genome sequences are deposited in the NCBI GenBank database under the bioproject number PRJNA546126.
### Table 1
Patient, clinical and microbiological characteristics of bla\textsubscript{OXA-244} harbouring Escherichia coli in Heidelberg and Mannheim, Germany, 2019–2020 (n = 9)

| Patient number | Accession number\(^a\) | First detection | Detection on admission | Age group (years) | Migration / travel | Specimen\(^b\) | Colonisation | Infection | Serotype\(^c\) | MLST\(^d\) | Carbapenemase | fimH\(^e\) | Meropenem MIC (µg/mL)\(^f\) | CIM |
|----------------|------------------------|-----------------|-----------------------|------------------|-------------------|----------------|--------------|-----------|-------------|----------|----------------|--------|-------------------|-----|
| P1             | SAMN16521172           | Oct 2019        | Yes                   | 10               | No                | Rectal swab    | +            | −         | O16:H5      | ST131    | OXA-244        | 41     | 0.125\(^g\)       | +   |
| P2             | SAMN16521173           | Jan 2020        | No                    | 10               | No                | Rectal swab, urine | +            | +         | O16:H5      | ST131    | OXA-244        | 41     | 0.75\(^h\)       | +   |
| P3             | SAMN16521174           | Dec 2019        | No                    | ≥70              | Libya\(^i\)      | Rectal swab, urine, blood culture | +            | +         | O16:H5      | ST131    | OXA-244        | 41     | 6\(^e\)          | +   |
| P4             | SAMN16521175           | Sep 2019        | Yes                   | 40–50            | Unknown          | Rectal swab    | +            | −         | O86:H14      | ST38     | OXA-244        | −      | 0.5              | +   |
| P5             | SAMN16521176           | Dec 2019        | Yes                   | 40–50            | No                | Rectal swab    | +            | −         | O86:H14      | ST38     | OXA-244        | −      | 0.19             | +   |
| P6             | SAMN16521177           | Mar 2020        | Yes                   | 20–30            | Unknown          | Rectal swab    | +            | −         | O102:H6      | ST38     | OXA-244        | 5      | 0.75             | +   |
| P7             | SAMN16521178           | May 2020        | No                    | 10               | No                | Rectal swab    | +            | +         | O153:H30     | ST38     | OXA-244        | 5      | 0.38             | +   |
| P8             | SAMN16521179           | Dec 2019        | No                    | 20–30            | No                | Rectal swab, urine | +            | +         | O86:H18      | ST38     | OXA-244        | −      | 0.5              | +   |
| P9             | SAMN16521180           | Jul 2020        | Yes                   | 60–70            | Unknown          | Rectal swab    | +            | −         | O101:H17     | ST167    | OXA-244 + NDM-5 | −      | 4\(^h\)          | +   |

CIM: carbapenem inactivation assay; MIC: minimum inhibitory concentration; MLST: multilocus sequence type; +: positive; −: negative.

\(^a\) Sequences were deposited in the Genbank at NCBI under the Bioproject PRJNA546126.

\(^b\) First detection specimen is underlined, in cases with multiple samples. Only the first isolate of each patient was sequenced.

\(^c\) Serotype was derived from the assembled draft genome using the CGE Serotype Finder 2.0 (https://cge.cbs.dtu.dk/services/SerotypeFinder/).

\(^d\) MLST derived from the assembled draft genome using CGE FimTyper 1.0 (https://cge.cbs.dtu.dk/services/FimTyper/).

\(^e\) fimH typing was derived from the assembled draft genome using the CGE Serotype Finder V2.0.

\(^f\) Meropenem MIC was determined using an agar-based gradient diffusion test (E-test).

\(^g\) E-test exhibited slight growth within the zone of inhibition.

\(^h\) Patient was in Libya prior to detection of OXA-244 producing E. coli.
**Figure 1**

Antimicrobial resistance genes in OXA-244-producing *Escherichia coli* in the Rhine-Neckar region, Germany, 2019–2020 (n = 9)

| ST: sequence type. |
|---|
| **Black squares**: presence, **grey squares**: absence of antimicrobial resistance genes; **red font and red squares**: carbapenemase genes. |

| Gene | ST131 | ST38 | ST167 |
|------|-------|-------|-------|
| aac(3)-IId | | | |
| aac(3)-IIe | | | |
| AAC(6')-Ib-cr | | | |
| aac-IVa | | | |
| aadA1-pm | | | |
| aadA5 | | | |
| acrD | | | |
| aph(3'')-Ib | | | |
| aph(4)-Ia | | | |
| aph(6)-Id | | | |
| kdpE | | | |
| CMY-59 | | | |
| TEM-1 | | | |
| ble-MBL | | | |
| NDM-5 | | | |
| OXA-244 | | | |
**Table 2**

Antibiotic susceptibility profile of *bla*<sub>OXA-244</sub>-harbouring *Escherichia coli* in the Rhine-Neckar region, Germany, 2019–2020 (n = 9)

| Substance                  | ST<sub>T31</sub> | ST<sub>T38</sub> | ST<sub>T167</sub> |
|----------------------------|------------------|------------------|-------------------|
|                            | P1   | P2   | P3   | P4   | P5   | P6   | P7   | P8   | P9   |
|                            | MIC  | Int  | MIC  | Int  | MIC  | Int  | MIC  | Int  | MIC  | Int  |
| Piperacillin/tazobactam    | ≥ 128 | R    | ≥ 128 | R    | ≥ 128 | R    | ≥ 128 | R    | ≥ 128 | R    |
| Cefotaxim                  | ≥ 64  | R    | ≥ 64  | R    | ≥ 64  | R    | ≥ 64  | R    | ≥ 64  | R    |
| Ceftazidim                 | 8     | S    | 8     | S    | 8     | S    | 8     | S    | 8     | S    |
| Cefepim                    | 32    | S    | 32    | S    | 16    | R    | 16    | R    | 16    | R    |
| Ceftolozan/tazobactam     | 4     | S    | 4     | S    | 4     | S    | 4     | S    | 4     | S    |
| Imipenem                   | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    |
| Meropenem                  | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    |
| Ciprofloxacin              | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    | ≤ 0.25 | S    |
| Trimethoprim/sulfamethoxazole | ≥ 320 | R    | ≥ 320 | R    | ≥ 320 | R    | ≥ 320 | R    | ≥ 320 | R    |
| Gentamicin                 | ≤ 1   | S    | ≤ 1   | S    | ≤ 1   | S    | ≤ 1   | S    | ≤ 1   | S    |
| Tobramycin                 | ≤ 1   | S    | ≤ 1   | S    | ≤ 1   | S    | ≤ 1   | S    | ≤ 1   | S    |
| Amikacin                   | 2     | S    | 2     | S    | 2     | S    | 2     | S    | 2     | S    |
| Tigecyclin                 | ≤ 0.5 | S    | ≤ 0.5 | S    | ≤ 0.5 | S    | ≤ 0.5 | S    | ≤ 0.5 | S    |
| Aztreonam                  | ≥ 64  | R    | ≥ 64  | R    | ≥ 64  | R    | ≥ 64  | R    | ≥ 64  | R    |
| Fosfomycin                 | ≤ 16  | S    | ≤ 16  | S    | ≤ 16  | S    | ≤ 16  | S    | ≤ 16  | S    |
| Colistin<sup>a</sup>       | ≤ 0.5 | S    | ≤ 0.5 | S    | ≤ 0.5 | S    | ≤ 0.5 | S    | ≤ 0.5 | S    |

I: intermediate; Int: interpretation; MIC: minimum inhibitory concentration in mg/L; R: resistant; S: susceptible; ST: sequence type.

MIC was determined by VITEK2 using the AST-N389 test panel. Antibiotic susceptibility was interpreted using the EUCAST clinical breakpoints v10.0 [7].

<sup>a</sup> Interpretation and MIC for colistin using VITEK2 may not be reliable [28].
Figure 2
Genetic characteristics of bla\textsubscript{OXA-244}—harbouring Escherichia coli in the Rhine-Neckar region, Germany, 2019–2020 (n = 9)

A. Clustering by the genetic environment of the bla\textsubscript{OXA-244} gene revealed two clusters. We were not able to identify any transposable elements within the contig of the assembled draft genome. Isolates belonging to the ST131 E. coli are indicated in red, ST38 in blue and ST167 in green font, corresponding to the figure legend of the minimum-spanning tree in panel C.

B. The analysis of the coverage in comparison to other contigs in the assembled draft genome suggests a chromosomal integration of the bla\textsubscript{OXA-244} gene in almost all isolates. Red vertical bars represent the bla\textsubscript{OXA-244}-containing contig.

C. Minimum-spanning tree based on the core genome of all sequenced E. coli in this study. Potential transmission clusters are indicated by the grey circles with SNP differences over the core genome in blue. There was no indication of patient-to-patient transmission (3,413 genes, 108,017 polymorphic sites). Numbers in square brackets indicate the number of isolates belonging to the MLST.

MLST: multilocus sequence type; SNP: single-nucleotide polymorphism.
Molecular and microbiological characteristics of OXA-244-producing Escherichia coli

Between January 2019 and June 2020, we identified 50 E. coli with phenotypic carbapenem resistance, of which 41 carried a carbapenemase. Nine of the 41 carried bla_{OXA-244}, which belonged to three clonal lineages ST38 (n = 5), ST131 (n = 3) and ST167 (n = 1). The isolate belonging to ST167 harboured two carbapenemase genes, bla\_NDM-1 and bla\_OXA-244. Relevant clinical and microbiological characteristics of the nine patients are summarised in Table 1.

The presence of genotypic antibiotic resistance determinants is summarised in Figure 1. Antibiotic susceptibility of all bla\_OXA-244 is displayed in Table 2. Isolates of the ST38 lineage carried variable extended-spectrum \(\beta\)-lactamase (ESBL) genes, such as bla\_CTX-M-14, bla\_CTX-M-23, and bla\_TEM-1, whereas all isolates of the ST131 clonal lineage harboured bla\_CTX-M-15 in addition to the bla\_OXA-244 gene (Figure 1).

Consistent with published data, the bla\_OXA-244 genes are most likely to have been integrated into the chromosome because sequencing coverage of the blaOXA-244-containing contigs was lower than the overall average sequencing coverage (Figure 2A and 2B) [5,15].

Seven of nine isolates were susceptible to meropenem as indicated by the low MIC in two different AST methods (Tables 1 and 2). One isolate (ST167, P9) carried both bla\_OXA-244 and bla\_NDM-1, so that high MIC values for carbapenem were expected. However, the isolate from P3 exhibited an unusually high MIC for meropenem for an OXA-244 producer in both AST methods (≥ 16 mg/L in VITEK and 6 mg/L in E-test) (Tables 1 and 2), for reasons we could not explain. Nevertheless, all nine isolates exhibited positive results in the phenotypic carbapenem inactivation assay (CIM) using meropenem disk (10 \(\mu\)g) with a 2 h inactivation step [16]. Our findings suggest that CIM may be a reliable method to detect OXA-244 producers and should be validated in further studies.

Potential origin and nosocomial transmission of OXA-244-producing ST131 Escherichia coli

SNP analysis to evaluate the clonal relationship of the isolates suggested two potential transmission clusters of patients P1-P2 with five SNP and P4-P5-P8 with 15-24 SNP (Figure 2C). Patient P1 was colonised with bla\_OXA-244 E. coli on admission. There was no recent travel exposure so that community acquisition in Germany was possible. P2 stayed in the same ward as P1 with some temporal overlap. P2 was born in the hospital and acquired the colonisation with ST131 OXA-244-producing E. coli during the hospital stay. Nosocomial transmission is a very likely source of acquisition as suggested by the identical genotypic and phenotypic resistance of both isolates of P1 and P2 (Figure 1 and Table 2). P3 was in a different hospital than P1 and P2. The lack of epidemiological link is consistent with the genomic analysis, which did not indicate transmission. P3 had had contact with the healthcare system in Libya and was initially screened negative on admission in Germany. The bla\_OXA-244 E. coli was detected in subsequent screenings. However, we cannot fully rule out importation because the sensitivity of the detection method is limited [15].

In the ST38 cluster, there was no epidemiological overlap so that a nosocomial patient-to-patient transmission event is unlikely. Nevertheless, community transmissions caused by clonal dissemination of bla\_OXA-244-positive ST38 E. coli in Germany cannot be entirely ruled out [17].

Discussion

The increased incidence in Europe of community-acquired infections with E. coli carrying OXA-244 is of public health relevance as reflected by the rapid risk assessment by the European Centre for Disease Prevention and Control (ECDC) at the beginning of 2020 [18]. Recently, several federal states in Germany reported a rise in detection of community-acquired infections with ST38 OXA-244-producing E. coli [17]. Similar observations have been reported in other European countries [4,5,19-21].

In Germany and other neighbouring countries in Europe, bla\_OXA-244 is predominantly found in ST38 E. coli [4,17,19,21,22]. Surveillance data from Denmark and France reported the presence of bla\_OXA-244 in other clonal groups (ST10, ST38, ST69, ST167, ST16, ST361, and ST 3268) [21,23], but to the best of our knowledge the presence of bla\_OXA-244 in ST131 E. coli in Europe has not been reported before. Besides being responsible for serious extra-intestinal infections, the development of resistance to carbapenems in the ST131 E. coli clonal lineage, is particularly worrisome as carbapenems are often the last line of therapy for life-threatening infections [2,24]. There are no systematic data on the prevalence of carbapenemase-producing Gram-negative bacteria in the Rhine-Neckar region. However, our data suggest a low prevalence of 0.5% (131/27,387 screened patients in the Heidelberg University Hospital in 2019), which is consistent with published data [25].

Peirano et al. reported that the global incidence of carbapenemase-producing E. coli ST131 O25b:H4 of the fimH30/virotype C lineage is increasing, with bla\_KPC as the most common carbapenem-resistance determinant [2]. In contrast, our E. coli ST131 has the serotype O16:H5 with bla\_OXA-244 that belongs to the fimH41/virotype C lineage [26]. Although the major lineage of the highly virulent ST131 belongs to the serotype O25b:H4 and fimH30, a murine infection model suggested that ST131 O16:H5 fimH41 is comparable to the H30 lineage in virulence and lethality [27], which implies that the emergence of carbapenem resistance in the H41 ST131 lineage is equally relevant.
Our study has limitations, the detection of OXA-244 producing *E. coli* is a major diagnostic challenge owing to its low level of phenotypic resistance to carbapenems; therefore OXA-244 producers may be underreported. Nevertheless, our finding suggests that a simple phenotypic assay for carbapenem inactivation combined with routine WGS may be useful to detect low carbapenemase producers, such as OXA-244. In addition, the epidemiological data of our patients were limited so that the exact origin of the OXA-244-producing ST131 *E. coli* in this study cannot be fully elucidated.

**Conclusion**

The emergence and dissemination of virulent and dominant *E. coli* clones with resistance to last-line antibiotics is a public health concern. Our findings emphasise the necessity of adequate surveillance measures and warrant further studies on the epidemiology and transmission dynamics of carbapenem-resistant *E. coli* both in the hospital and community setting.

**Ethical statement**

Data and isolates were collected and characterised in accordance to the German Infection Protection Act. The local ethical committee was consulted for the usage of clinical data for scientific purposes and granted waiver of informed consent (S-474/2018).

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**Conflict of interest**

None declared.

**Authors’ contributions**

SW, SB, TM, KH, DN performed the clinical data analysis and visualisation. SB performed the analysis of WGS data. All authors were involved in the design and conception of the study. All authors approved the final version of the manuscript.

**References**

1. Nicolas-Chanoine MH, Bertrand X, Madec JY. Escherichia coli ST313, an intriguing clonal group. Clin Microbiol Rev. 2014;27(3):543-74. https://doi.org/10.1128/CMR.00125-13 PMID: 24893211
2. Peirano G, Bradford PA, Kazmierczak KM, Badal RE, Hackel M, Hoban DJ, et al. Global incidence of carbapenemase-producing Escherichia coli ST313. Emerg Infect Dis. 2014;20(11):1928-31. https://doi.org/10.3201/eid2014.140738 PMID: 25340464
3. Poirel L, Potron A, Nordmann P. OXA-48-like carbapenemases: the phantom menace. J Antimicrob Chemother. 2012;67(7):1507-606. https://doi.org/10.1093/jac/dks121 PMID: 22499966
4. Masseron A, Poirel L, Falgenhauer L, Imirzalioglu C, Kissler J, Chakraborty T, et al. Ongoing dissemination of OXA-244 carbapenemase-producing Escherichia coli in Switzerland and their detection. Diagn Microbiol Infect Dis. 2020;97(3):115059. https://doi.org/10.1016/j.diagmicrobio.2020.115059 PMID: 33387846
5. Potron A, Poirel L, Dortet L, Nordmann P. Characterisation of OXA-244, a chromosomally-encoded OXA-48-like β-lactamase from Escherichia coli. Int J Antimicrob Agents. 2016;47(1):102-3. https://doi.org/10.1016/j.ijantimicag.2015.10.014 PMID: 26655033
6. Kocer K, Boutin S, Dalipe AH, Heeg K, Muters NT, Nurjadi D. Comparative genomic analysis reveals a high prevalence of inter-species in the transfer of carbapenem-resistance plasmids in patients with haematological malignancies. Clin Microbiol Infect. 2020;26(6):780-8.e1-8. https://doi.org/10.1016/j.clinmicinfection.2020.01.014 PMID: 31567799
7. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 10.0, 2020. Available from: http://www.eucast.org/clinical_breakpoints/REMOVED IF FIELD
8. Bankevich A, Nurk S, Antipov D, Gurevich AA, Dvorkin M, Kulikov AS, et al. SPAdes: a new genome assembly algorithm and its applications to single-cell sequencing. J Comput Biol. 2012;19(5):455-77. https://doi.org/10.1089/cmb.2012.0021 PMID: 22506549
9. Page AJ, Cummins CA, Hunt M, Wong VK, Reuter S, Holden MT, et al. Roary: large-scale rapid prokaryote pan genome analysis. Bioinformatics. 2015;31(22):3691-3. https://doi.org/10.1093/bioinformatics/btv460
10. Seemann T. Prokka: rapid prokaryotic genome annotation. Bioinformatics. 2014;30(14):2068-9. https://doi.org/10.1093/bioinformatics/btu153 PMID: 24842063
11. Feldmeyer G, Brover V, Haft DH, Prasad AB, Slotta DJ, Tostloy I, et al. Validating the AMRFinder tool and resistance gene database by using antimicrobial resistance genotype-phenotype correlations in a collection of isolates. Antimicrob Agents Chemother. 2019;63(1):e00483-19. https://doi.org/10.1128/AAC.00483-19 PMID: 31427293
12. Jia B, Raphenya AR, Alcock B, Waglechner N, Guo P, Tsang KK, et al. CARD 2017: expansion and model-centric curation of the comprehensive antibiotic resistance database. Nucleic Acids Res. 2017;45(D1):D66-73. https://doi.org/10.1093/nar/gkw1004 PMID: 27789705
13. Gupta SK, Padmanabhan BR, Diene SM, Lopez-Rojas R, Kempf M, Landraud L, et al. ARG-ANNOT, a new bioinformatic tool to discover antibiotic resistance genes in bacterial genomes. Antimicrob Agents Chemother. 2014;58(1):212-20. https://doi.org/10.1128/AAC.01310-13 PMID: 24455322
14. Zankari E, Hasman H, Cosentino S, Vestergaard M, Rasmussen JK, Brasso WB, et al. Modified carbapenem inactivation method for phenotypic detection of carbapenemase production among Enterobacteriaceae. J Clin Microbiol. 2017;55(8):2321-33. https://doi.org/10.1128/JCM.00493-17 PMID: 28186009
15. Hoyo-Mallecot Y, Naas T, Bonnin R, Patino R, Glaser P, Fortiniou N, et al. OXA-244-producing Escherichia coli isolates, a challenge for clinical microbiology laboratories. Antimicrob Agents Chemother. 2017;61(9):e00818-17. https://doi.org/10.1128/AAC.00818-17 PMID: 28675064
16. Pierce VM, Simmer PJ, Lonswar DR, Roe-Carpenter DE, Johnson JK, Brasco WB, et al. Identification of acquired antimicrobial resistance genes. J Antimicrob Chemother. 2012;67(11):2640-4. https://doi.org/10.1093/jac/dks261 PMID: 22782487
17. Kremer K, Kramer R, Neumann B, Hailer S, Pfennigwerth N, Werner G, et al. Rapid spread of OXA-44-producing Escherichia coli ST38 in Germany: insights from an integrated molecular surveillance approach; 2017 to January 2020. Euro Surveill. 2020;25(25):2000923. https://doi.org/10.2807/1560-7917.EU.2020.25.20.2000923 PMID: 32613940
18. European Centre for Disease Prevention and Control (ECDC). Rapid risk assessment: Increase in OXA-244-producing Escherichia coli in the European Union/European Economic Area and the UK since 2013. Stockholm: ECDC; 18 Feb 2020. Available from: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-increase-oxa-244-producing-escherichia-coli-eua-era
19. Fursova NK, Astashkin EI, Knyazeva AI, Kartsev NN, Leonova ES, Ershova ON, et al. The spread of bla OXA-48 and bla OXA-244 carbapenemases genes among Klebsiella pneumoniae, Proteus mirabilis and Enterobacter spp. isolated in Moscow, Russia. Ann Clin Microbiol Antimicrob. 2015;14(1):46. https://doi.org/10.1186/s12934-015-0108-y PMID: 26526183
20. Oteo J, Hernández JM, Espasa M, Fleites A, Sáez D, Bautista V, et al. Emergence of OXA-48-producing Klebsiella pneumoniae and the novel carbapenemases OXA-244 and OXA-245 in Spain. J Antimicrob Chemother. 2013;68(2):317-21. https://doi.org/10.1093/jac/dkt383 PMID: 23034714
21. Hammerum AM, Porsbo LJ, Hansen F, Roer L, Kayh A, Henius A, et al. Surveillance of OXA-244-producing Escherichia coli and epidemiologic investigation of cases, Denmark, January 2016 to August 2019. Euro Surveill. 2020;25(18). https://doi.org/10.2807/1560-7917.EU.2020.25.18.1900742 PMID: 32400363
22. Falgenhauer L, Nordmann P, Imirzalioglu C, Yao Y, Falgenhauer J, Hauri AM, et al. Cross-border emergence of clonal...
lineages of ST38 Escherichia coli producing the OXA-48-like carbapenemase OXA-244 in Germany and Switzerland. Int J Antimicrob Agents. 2020;106157. https://doi.org/10.1016/j.ijantimicag.2020.106157 PMID: 32919009

23. Émeraud C, Biez L, Girlich D, Jousset AB, Naas T, Bonnin RA, et al. Screening of OXA-244 producers, a difficult-to-detect and emerging OXA-48 variant? J Antimicrob Chemother. 2020;75(8):2120-3. https://doi.org/10.1093/jac/dkaa155 PMID: 32363407

24. Pitout JD. Extraintestinal pathogenic Escherichia coli: an update on antimicrobial resistance, laboratory diagnosis and treatment. Expert Rev Anti Infect Ther. 2012;10(10):1165-76. https://doi.org/10.1586/eri.12.110 PMID: 23199402

25. Albiger B, Glasner C, Struelens MJ, Grundmann H, Monnet DL, European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) working group. Carbapenemase-producing Enterobacteriaceae in Europe: assessment by national experts from 38 countries, May 2015. Euro Surveill. 2015;20(45):30062. https://doi.org/10.2807/1560-7917.ES.2015.20.45.30062 PMID: 26675038

26. Dahbi G, Mora A, Mamani R, López C, Alonso MP, Marzoa J, et al. Molecular epidemiology and virulence of Escherichia coli O16:H5-ST131: comparison with H30 and H30-Rx subclones of O25b:H4-ST131. Int J Med Microbiol. 2014;304(8):1247-57. https://doi.org/10.1016/j.ijmm.2014.10.002 PMID: 25455219

27. Mora A, Dahbi G, López C, Mamani R, Marzoa J, Dion S, et al. Virulence patterns in a murine sepsis model of ST131 Escherichia coli clinical isolates belonging to serotypes O25b:H4 and O16:H5 are associated to specific virotypes. PLoS One. 2014;9(1):e87025. https://doi.org/10.1371/journal.pone.0087025 PMID: 24498015

28. Matuschek E, Åhman J, Webster C, Kahlmeter G. Antimicrobial susceptibility testing of colistin - evaluation of seven commercial MIC products against standard broth microdilution for Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Acinetobacter spp. Clin Microbiol Infect. 2018;24(8):865-70. https://doi.org/10.1016/j.cmi.2017.11.020 PMID: 2922199

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