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# P1209 Extended-spectrum beta-lactamse-producing strains among clinical isolates of *Escherichia coli* and *Klebsiella pneumoniae* from hospitalised patients in Germany, 2012-2016

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**Background:** The treatment of infectious diseases caused by *Escherichia coli* (ECO) and *Klebsiella pneumoniae* (KPN) has increasingly been threatened by the emergence and dissemination of ESBL-producing strains. The objectives of this study were i) to evaluate the occurrence of ESBL-producing strains among clinical isolates of ECO and KPN obtained from hospitalized patients, ii) to identify the ESBL genes and antimicrobial resistance patterns in these isolates, and iii) to investigate the presence of major clonal lineages among ESBL-producing isolates.

**Materials/methods:** Isolates were collected prospectively at 18 medical centres in Germany over a three-month-period in the years 2010, 2013 and 2016. Verification of species identification and susceptibility testing were performed in one reference laboratory. MICs of antimicrobial agents were determined by broth microdilution according to the ISO-standard and interpreted by EUCAST criteria (v.8.1). Isolates with a confirmed ESBL phenotype were characterized by PCR amplification and sequencing of *bla* genes. Furthermore, the prevalence of major clonal lineages among ESBL-producing isolates was investigated by whole genome sequencing (Illumina, MiSeq).

**Results:** 1.167 / 625 isolates of ECO / KPN were collected, of which 66 (17.1%) / 31 (14.9%), 63 (15.8%) / 36 (16.9%) and 77 (20.2%) / 34 (16.7%) showed an ESBL phenotype in 2010 (n=387/208), 2013 (n=398/213) and 2016 (n=382/204), respectively. Genes encoding CTX-M-ESBLs were confirmed for 61 / 25, 59 / 31, and 75 / 34 of ECO / KPN isolates in 2010, 2013, and 2016, respectively. In all years, the predominant CTX-M-type ESBL was CTX-M-15 (ECO appr. 50%; KPN, >90%). With regards to resistance patterns, about 60-80% of the CTX-M-producing strains were cross-resistant each to ciprofloxacin and trimethoprim/sulfamethoxazole (Table). The proportion of CTX-M-producing ECO belonging to the clonal lineage ST131 inreased from 17/61 (27.5%) in 2010 to 36/75 (48%) in 2016 ($p<0.01$). Leading clonal lineages among CTX-M-producing KPN in 2016 were ST-15 (17.6%), ST-219 and ST-307 (each 11.8%).

**Conclusions:** Overall, the level of ESBL-producing isolates among ECO and KPN from hospitalized patients remained stable between 2010 and 2016. The proportion of CTX-M-producing strains belonging to high-risk clone ST131 among ECO isolates, however, increased from 4.5% in 2010 to 9.3% in 2016.

**Table: Number (%) of CTX-M-producing *E. coli* and *K. pneumoniae* isolates resistant to selected antimicrobial agents by year of collection**

| Antibacterial agent | *E. coli* | | | | *K. pneumoniae* | | | |
|---|---|---|---|---|---|---|---|---|
| | 2010 (n=61) | 2013 (n=59) | 2016 (n=75) | Trend [a] | 2010 (n=25) | 2013 (n=31) | 2016 (n=34) | Trend [a] |
| Amoxicillin/ clavulanic acid | 50 (82) | 48 (81.4) | 42 (56) | 0.0006 | 24 (96) | 29 (93.5) | 26 (76.5) | 0.0181 |
| Piperacillin/ tazobactam | 12 (19.7) | 9 (15.3) | 9 (12) | 0.2189 | 7 (28) | 12 (38.7) | 9 (26.5) | 0.8206 |
| Meropenem | 0 (0) | 0 (0) | 0 (0) | n/a | 0 (0) | 0 (0) | 0 (0) | n/a |
| Amikacin | 1 (1.6) | 0 (0) | 0 (0) | 0.1965 | 0 (0) | 0 (0) | 0 (0) | n/a |
| Gentamicin | 20 (32.8) | 21 (35.6) | 21 (28) | 0.5236 | 14 (56) | 18 (58.1) | 16 (47.1) | 0.4615 |
| Tobramycin | 27 (44.3) | 21 (35.6) | 24 (32) | 0.1451 | 13 (52) | 11 (35.5) | 10 (29.4) | 0.0833 |
| Ciprofloxacin | 46 (75.4) | 40 (67.8) | 57 (76) | 0.8865 | 20 (80) | 25 (80.6) | 23 (67.6) | 0.246 |
| Trimethoprim/ sulfamethoxazole | 37 (60.7) | 40 (67.8) | 44 (58.7) | 0.7648 | 14 (56) | 23 (74.2) | 30 (88.2) | 0.0052 |
| Fosfomycin [b] | 3 (4.9) | 2 (3.4) | 2 (2.7) | 0.487 | 9 (36) | 4 (12.9) | 15 (44.1) | 0.3645 |
| Colistin | 0 (0) | 0 (0) | 1 (1.3) | 0.2634 | 3 (12) | 1 (3.2) | 1 (3) | 0.1522 |

[a] Chi-squared-test for linear trend; p value; [b] Note, that we used broth microdilution which is not the reference method of susceptibility testing for fosfomycin; n/a, not applicable

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