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Outbreak due to an extensively drug-resistant Klebsiella pneumoniae harbouring blaNDM-1 and/or blaOXA-48 in Barcelona, Spain

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Background: The first enterobacteriaceae producing *bla*$_{NDM-1}$ detected in Spain was reported in 2011. Since then, sporadic detections from different regions were published, including a small outbreak from Madrid. Here, we report an outbreak due to a ST147 *Klebsiella pneumoniae* producing *bla*$_{NDM-1}$ and/or *bla*$_{OXA-48}$ in Barcelona, Spain.

Material/methods: The outbreak took place at Hospital Universitari de Bellvitge, an adult's teaching hospital (600 beds). Isolates were obtained from the active surveillance program (rectal swabs) and/or clinical samples from October 2015 to 2016. Rectal swabs were inoculated in an enrichment broth, incubated and plated on a selective agar (ChromID). All growing isolates were identified by MALDI-

TOF MS (MALDI-Biotyper®) and tested for antimicrobial susceptibility by microdilution (MicroScan®). The carbapenemase activity was screened through the modified Hodge test with imipenem. All positive isolates were studied by PCR (targeting *bla*$_{OXA-48}$, *bla*$_{VIM}$, *bla*$_{NDM-1}$ and *bla*$_{KPC}$) and genotyped by PFGE (*XbaI*). A selection of isolates was further studied using whole genome sequencing (WGS, Illumina). A multi-disciplinary team was set up to supervise and improve the screening detection, patient's isolation and cleaning measures.

Results: The index case was detected in October 2015 and was confirmed as a carrier of an extensively-drug resistant *K. pneumoniae* producing *bla*$_{NDM-1}$. That strain was resistant to all tested antimicrobials with exception of tigecycline (MIC 2 mg/L), fosfomycin (MIC 64 mg/L) and colistin (MIC<2 mg/L). During the study period, 5914 rectal swabs (2834 patients) were screened. A total of 119 patients, whose *K. pneumoniae*-*bla*$_{NDM-1}$ and/or *bla*$_{OXA-48}$ isolates shared the same PFGE pattern, were detected. Among them, three carbapenemase production patterns were found: *bla*$_{NDM-1}$ (n=7, 6%), *bla*$_{NDM-1+OXA48}$ (n=59, 50%) and *bla*$_{OXA-48}$ (n=22, 18%); 31 (26%) patients showed more than one pattern. The active surveillance program detected 98 (82%) patients and 21 were detected by a positive clinical sample. Overall, 40 (34%) patients presented a clinical sample, including 10 patients (9%) with bacteraemia. As deduced by WGS, the first strain belonged to ST147 and harboured several resistance mechanisms including *bla*$_{NDM-1}$, *bla*$_{CTX-M-15}$, *bla*$_{SHV11}$, *RmtF, aph(3')-Ia, aacA4, QnrB66, oqxA, oqxB, aac(6')Ib-cr, fosA, mph(A), arr-2, sul1, dfrA14 and dfrA12*. During the outbreak, the initial *K. pneumoniae*-*bla*$_{NDM-1}$ strain acquired a *bla*$_{OXA-48}$ and, later, a second event led to a *bla*$_{NDM-1}$ loss. Colistin-resistance was detected in 13 (11%) patients (*mcr-1* negative). Briefly, outbreak control measures included active surveillance, reinforcement of isolation/cohorting policies and enhanced environmental cleaning. The outbreak's peak occurred in August 2016 (detection of 28 patients). Although the last patient carrying a ST147-b*la*$_{NDM-1}$ strain was detected in October 2016, the ST147-*bla*$_{OXA-48}$ detection remains active.

Conclusions: We describe the introduction of a high risk clone which rapidly spread over the hospital. The active surveillance program is essential in order to detect the hidden carriers and to establish effective control measures.