# Ongoing outbreak due to *Klebsiella pneumoniae* OXA-48 in an Italian referral hospital

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**INTRODUCTION** The 2014 ECDC Surveillance data confirmed that carbapenem resistance among *Klebsiella pneumoniae* isolates is due to beta-lactamases belonging to the KPC, VIM or OXA- 48 families. Italy is at a high-level endemicity of carbapenem-resistant *Klebsiella pneumoniae* and KPC, and is by far the most widespread mechanism of resistance, accounting for >90% of the strains. Despite these data, Trieste Hospital is sited in a low-endemicity CRE area, accounting only for the 7% of the strains. Until September 2015 the only mechanism described in CR *Klebsiella pneumoniae* was KPC.

The **OXA-48** mechanism has been **reported very rarely in Italy** and only for sporadic cases.

We describe in this poster an **outbreak of the OXA-48 producing *Klebsiella pneumoniae*** strain, the first in our country.

**MATERIAL/METHODS** The bacterial identification was performed by Vitek-2 (bioMérieux).

Minimal inhibitory concentrations (MICs) were determined by Vitek-2 and/or by a micro-dilution method (Sensititre Diagnostic System, Trek), and interpreted according to the EUCAST criteria.

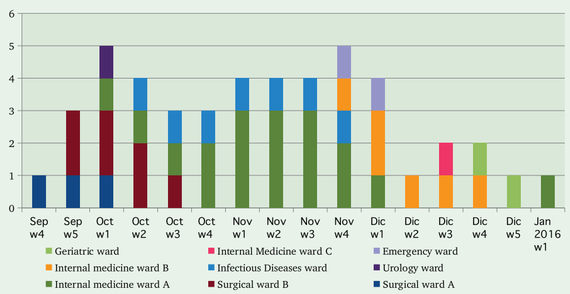
The mechanism of carbapenem resistance was confirmed by a Real Time PCR method which allows the detection of the $bla_{OXA-48}$, $bla_{VIM}$, $bla_{IMP-1}$, $bla_{NDM}$ and $bla_{KPC}$ carbapenemase genes.

Genotyping to determine genetic relatedness between isolates was performed by analysis of pulsed-field gel electrophoresis (PFGE) profiles of chromosomal DNA digested with XbaI.

**RESULTS** At the beginning of September 2015 a patient underwent a cholecystectomy and after 20 days he needed a CT-driven drainage at the surgical site. We isolated an MDR *Klebsiella pneumoniae* strain from drained liquid, subsequently identified as an OXA-48 producer. Then in the following 3 months, until the first week of January 2016, another 13 MDR OXA-48 producers *Klebsiella pneumoniae* strains (OXA-48-Kp) were isolated in our hospital, all from clinical specimens. The outbreak was initially confined to the Surgical Department, but the it soon spreaded to the Medical Wards and eventually to the Emergency Department and to the Geriatric Ward (the Infectious Diseases Ward was involved only because they received an infected patient from the Surgical Department).

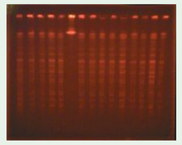
Soon after the first isolate, the OXA-48-Kp strain was found in another four patients, two in the **Surgical Department** (both in ct-driven drained liquids) and two in the **Medical Wards** (colonizations). After two weeks we discovered another case in a Medical Ward, and then, at the end of November 2015 we found four other cases, all in the Medical Wards (one in a blood culture, one from a BAL and two from colonizations). Thereafter, 4 colonized patients were detected in two Medical Wards and in the Geriatric Ward between the second week of December and the first week of January.

Up until now, no other cases were reported.




Trends of OXA 48 cases in different hospital wards, from the 4th week of September 2015 to January 2016

All the isolates were resistant to penicillins +/- beta-lactamase inhibitors, cephalosporins, levofloxacin, ciprofloxacin and meropenem; most of them (except one, which was restistant to) were intermediate for imipenem, and all of them were susceptible to amikacin, trimethoprim/sulfamethoxazole and colistin. The resistance profile suggested the presence of an ESBL mechanism associated to OXA-48. One of the infected patients received colistin, tigecyclin and meropenem for 3 days (the therapy was then switched to meropenem plus ertapem due to facial edema and acute kidney failure), but this was enough to induce resistance to colistin in the OXA-48-Kp strain, hinting the presence of a repressed mechanism of resistance to colistin.



Pulsed-field gel electrophoresis (PFGE) profiles of chromosomal DNA digested with XbaI, lines 1-5 and 7- 15 corresponding to the single patients OXA-48-Kp strains, line 6 marker.

Pulse Field Gel Electophoresis showed a unique profile for all the strain, confirming that the outbreak was due to a **single clone**.

Among the patients involved in the outbreak, 7 had infections (50%), being found positive for the OXA-48-Kp in peritoneal drainage liquids and in the BAL. The other patients were colonized. All the cases were characterized as hospital-acquired, and none of them were linked to a history of travelling to endemic areas for OXA-48 producing *Klebsiella pneumoniae*. The average age of the patients was 75 years (+/- 17), and, as far as it was possible to find out, none of them had received antibiotic therapy in the previous 12 months. All the patients were admitted to the hospital for acute severe events. Five of the fourteen patients underwent for ERCP and/or EGDS before the OXA-48-Kp finding, but all the controls performed before, during and after the outbreak escluded any contamination of the instruments used.

At present, the original source of the outbreak has yet to be discovered.

**CONCLUSIONS** Trieste Hospital is located in a Region of low-level endemicity of carbapenem-resistant *Klebsiella pneumoniae*, and before September 2015 the only mechanism of resistance to carbapenems detected in *Klebsiella pneumoniae* had been KPC production. In this report we describe **the first outbreak of OXA-48 *Klebsiella pneumoniae* in Italy**, which lasted for about three months, from late September 2015 to early January 2016. It involved **fourteen patients**, both in Surgical and Medical wards and it was due to a **monoclonal strain**. Despite investigations, it was not possible to find out the source of the outbreak. A strong surveillance program had been carried out in almost all the wards involved, and probably the 'search and isolate' approach has been once again demonstrated to be en efficient tool to retain the spreading of CPE.

Sequencing of the strain is ongoing in order to determine the specific sequence type to whom the strain belongs.