

Dissemination of carbapenemase-producing *Enterobacteriaceae* at the Taher Sfar University Hospital, Mahdia, Tunisia

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INTRODUCTION

Carbapenem-Resistant-Enterobacteriaceae constitute an important public health. The most common mechanisms observed responsible of this resistance in Enterobacterial species are part of Ambler class A (KPC), B (VIM, IMP) and D (OXA-48-like) β -lactamases. Production of NDM β -lactamase is recent and appear in a widespread pattern in India, Pakistan, USA and Turkey. In Tunisia, resistance to carbapenem in *Enterobacteriaceae* is generally associated to the production of OXA-48-like β -lactamase. The present study was performed to investigate the molecular basis of carbapenem resistance in *Enterobacteriaceae* isolated in the University Hospital Tahar Sfar in Mahdia, Tunisia in a three year period.

Material and Methods

From 2013 to 2015, 10 Enterobacterial strains resistant to ertapenem according to EU-CAST guidelines were isolated from various clinical infections in several wards, including orthopaedics (3 isolates), intensive care unit (2 isolates), urology (1 isolates) and 1 isolate from the medicine, surgery, pediatric and pneumology wards, respectively. Isolates were identified by MALDI-TOF as *Klebsiella pneumoniae* strains. Antimicrobial susceptibility was performed by disc diffusion. Genetic characterization was performed by PCRs for the detection of bla_{CTX-M} , bla_{SHV} , bla_{KPC} , bla_{NDM} , bla_{IMP} , bla_{VIM} and bla_{OXA-48} . bla genes were sequenced and plasmids were characterized by rep-typing (Diatheva) and Southern blot on S1-PFGE gels. Clonality was assessed by PFGE and MLST.

Results

The PCR results showed that 8 strains harbored the $bla_{OXA-48-like}$ gene, 2 strains had the bla_{NDM-1} gene, whereas the bla_{KPC} , bla_{IMP} and bla_{VIM} genes were not detected. All isolates produced CTX-M-1 extended-spectrum- β -lactamase; sequencing lead to the identification of 7 CTX-M-15 and 3 CTX-M-1 producing strains. All strains but one harbour 3 plasmids of the IncL, IncFIK and IncR families. One strain (M4) has 1 plasmid of the IncX2 family. As demonstrated by S1 nuclease-Pulsed Field Gel Electrophoresis (S1-PFGE) and Southern blot experiments M6 and M10 isolates possessed an FIK plasmid harboring the bla_{NDM-1} gene.

Table: Characteristics of carbapenemase producing *Enterobacteriaceae* in the Taher Sfar University Hospital

Isolate	Isolation Date	Specimen	Ward	Sex	Carbapenemase and ESBL	Plasmid	Plasmid carrying bla_{NDM-1} gene	Sequence Type
M1	26/12/2012	Urine	Medicine	F	OXA-48-like, CTX-M15	R, FIK, L		ND
M2	24/10/2013	Catheter	Pediatric Unit	M	OXA-48-like, CTX-M15	R, FIK, L		ND
M3	29/11/2013	Urine	Surgery	F	OXA-48-like, CTX-M15	R, FIK, L		ND
M4	28/02/2015	Urine	Urology	F	OXA-48-like, CTX-M1	X2		ND
M5	05/03/2015	Pus	Intensive Care Unit	F	OXA-48-like, CTX-M1	R, FIK, L		ND
M6	09/03/2015	Urine	Intensive Care Unit	M	NDM-1, CTX-M-15	R, FIK, L	FIK	147
M7	13/04/2015	Urine	Orthopaedic	F	OXA-48-like, CTX-M15	R, FIK, L		ND
M8	20/04/2015	Pus	Orthopaedic	F	OXA-48-like, CTX-M15	R, FIK, L		ND
M9	02/05/2015	Pus	Orthopaedic	F	OXA-48-like, CTX-M15	R, FIK, L		ND
M10	16/05/2015	Urine	Pneumology	M	NDM-1, CTX-M1	R, FIK, L	FIK	147

CONCLUSION

Here, we report an increased prevalence of carbapenemase-producing *Enterobacteriaceae* in the University hospital Taher Sfar in Mahdia. This work highlights the ability of OXA-48-like carbapenemase to spread among enterobacteriaceae. This is also the first description of an ST 147 *K. pneumoniae* isolates carrying the bla_{NDM-1} gene in a Tunisian hospital. Finding are of great epidemiologic and clinical interest.