# Emerging extensively drug-resistant bacteria (eXDR) in an Algerian emergency hospital: characterization and recommendations

**M.Hamidi[1-4], H.Tali Maamar[2-4], N.Benamrouche[2-4], N.Aggoune[3-4], S.Bouheraoua[2], S.Nouar[1-4], B.Guettou[2], F.Assaous[2], N.Ait Hammou[1-4], K.Rahal[2-4]**

*[1]Central Laboratory of Biology, Emergency Hospital Salim Zemirli [2]Medical Laboratory of Bacteriology , Pasteur Institut of Algeria [3]Laboratory of Microbiology, Central Hospital of Army, [4]Laboratory of Microbiology, Faculty of Medecine, University of Algiers , Algeria*

## Introduction

➢Emerging Extensively Drug Resistant Bacteria (eXDR) is a worldwide menace to public health. These bacteria mainly concern carbapenemase-producing Enterobacteriaceae (CPE) and vancomycin-resistant enterococci (VRE) (*Enterococcus faecium* ++).

➢eXDR belonging to the commensal gastrointestinal tract flora are therefore likely to be carried for a long time and can potentially spread in hospitals and in the community.

## Aim

➢Frequency and molecular characteristics of eXDR (CPE and VRE) in our hospital during the years 2012-2014.

## Material and methods

➢A prospective study was conducted from January 2012 to December 2014. We collected 551 strains of *Klebsiella pneumoniae*, 257 strains of *Enterobacter cloacae* from a total of 2009 Enterobacteriacae and 201 strains of *Enterococcus* spp.

➢These isolates were recovered from different clinical samples ( blood culture, CRF, pus, BPS, urine, catheters..) providing from different departments (Surgery, Orthopaedics, ICU, Internal medicine, Neurosurgery) of the hospital.

**Table 1: Frequency per year of eXDR isolated in Emergency Hospital Salim Zemirli, Algiers, Algeria**

| | 2012 | 2013 | 2014 | Total |
|---|---|---|---|---|
| **ESBLE** | 123/612 | 102/598 | 175/799 | 400/2009 |
| **CPE** | 00/612 | 00/598 | 04/799 | 04/2009 |
| **VRE** | 00/54 | 00/56 | 01/91 | 01/201 |

➢Antimicrobial susceptibility was performed by diffusion method on agar medium and as recommended by the CLSI (2015).

➢Isolates were further tested to minimum inhibitory concentration (MIC) using the gradient strip E test.

➢Enterobacteriaceae with reduced susceptibility to ertapenem were tested for carbapenemases by modified Hodge test (MHT), Temocillin test and the test with EDTA. Determination of ESBL was carried out by the double-disc method.

➢For *Enterococcus* spp a screening test for vancomycin (6µg/ml) was done.

➢Detection of carbapenem and vancomycin resistance genes(*oxa48, kpc, ndm* and *van*) was performed by a multiplex PCR.

## Results

➢We found **05** eXDR: **CPE: 0.19%** [*K.pneumoniae* 0.55% (3/551), *E.cloacae* 0.39% (1/257)] and vancomycin resistant *E.faecium* 0.5% (1/201).

➢Modified Hodge test (MHT) was positive, Temocillin was <6mm and the test with EDTA was negative for all Enterobacteriaceae with reduced susceptibility to ertapenem.

➢All of these eXDR were isolated during 2014.The Molecular test showed that all carbapenemases were due to the presence of *bla*$_{oxa\text{-}48}$ gene alone and vancomycin resistance was due to the presence of the gene *vanA*.

## Conclusion

➢eXDR was found for the first time in our hospital in 2014. Low frequency was observed: **CPE 0,19%, VRE 0,5%.**

➢In our country Algeria **1.2%** of *K.pneumoniae* was resistant to Imipenem, **1.69%** of *Eterococcus* spp. was resistant to Vancomycin during 2014.

➢In Europe: 0.7 % of clinical Enterobacteriaceae isolates were resistant to carbapenem (Trans- Networks ONERBA) and <1 % of clinical isolates *E. faecium* were resistant to glycopeptides (ECDC 2011).

➢According to our results a regular monitoring of level of resistance in our hospital is required.

➢eXDR was detected from a clinical sample after few days of hospitalisation.

➢No contact isolation was prescribed at the admission.

**So we strongly recommend:**

•standard precautions regard to all health professionals caring for any patients

•isolation in single room for patients carrying eXDR ( contact precautions).

• Specific organization of healthcare.

•Limitation of transfers of patients in contact with the eXDR carrier.

•Digestive screening of patients in contact with the eXDR carrier.

•Excreta management.

•Reinforcing hand hygiene and bio-cleaning.

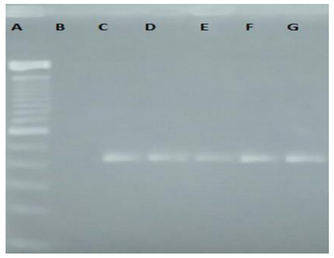


**Figure 1: PCR result detecting bla oxa -48**
A: 100 bp size marker ;
B: Negative control ;
C: Positive control( OXA- 48);
D: Strain S255 / 14;
E: Strain S18 / 15;
F: Strain S30 / 15
G: Strain S32 / 15.

**Table 2: Characteristics of CRE and VRE isolated in Emergency Hospital Salim Zemirli, Algiers, Algeria**

| N° Strain | Bacteria | Sex/age (y) | Department | sample | Sampling date | resistance gene | Antibiotic resistance profile | MIC (µg/ml) |
|---|---|---|---|---|---|---|---|---|
| **S225/14** | *Eterococcus faecium* | F/87 | Internal medicine | Wound pus | 14/04/2014 | *vanA* | AMP-GEN-STR-K-E-CM-QDA-FOS-LEV-TE-NIT-RIF-TEC- VA | VA= 256 TEC=48 |
| **S255/14** | *Klebsiella pneumoniae* | F/75 | Orthopaedics | BPS | 11/03/2014 | *bla*$_{OXA\text{-}48}$ | AMP-AMC-CZ- ETP- IPM- MEM-FOS | ETP=24 IPM=2 MEM=8 |
| **S18/15** | *Enterobacter cloacae* | M/ | ICU | Catheter | 12/01/2015 | *bla*$_{OXA\text{-}48}$ | AMP-AMC-CZ-CF-FOX-CTX-CAZ-FEP-AZT-ETP-GEN-TOB-CIP-SXT-NIT | ETP= 8 IPM=0.75 MEM=1 |
| **S30/15** | *Klebsiella pneumoniae* | M/21 | ICU | Urine | 03/12/2014 | *bla*$_{OXA\text{-}48}$ | AMP-AMC-CZ-CF-ETP-TE-SXT | ETP =1.5 IPM=0.75 MEM=0.38 |
| **S32/15** | *Klebsiella pneumoniae* | F/72 | ICU | BPS | 03/12/2014 | *bla*$_{OXA\text{-}48}$ | AMP-AMC-CZ-CF-CTX-CAZ-AZT-ETP-TE-GEN-TOB-CIP-SXT | ETP= 2 IPM=0.5 MEM=0.38 |

AMP : amoxicillin; AMC : amoxicillin/clavulanic acid; CF : cefalotin; CZ: cefazolin, FOX: cefoxitin, ETP : ertapenem , IPM: imipenem; MEM: meropenem,CTX : cefotaxim; CAZ : ceftazidim; FEP: cefepim, STR: streptomycin, TOB: tobramycin, NET: netilmicin; K: Kanamycin, GEN: gentamicin; SXT: sulfametoxazol-trimetoprim; AZT: aztreonam, FOS: fosfomycin,,CIP: ciprofloxacin, LEV: levofloxacin, E: erythromycin,, CM: clindamycin, QDA: quinopristin-dalfopristin, TE: tetracyclin, RIF: rifampicin, NIT: nitrofurantoine, Va: vancomycin, TEC: teicoplanin, ICU: intensive care unit, BPS: blinded protected specimen, CRF: cerebrospinal fluid. ESBLE: extended spectrum beta lactamase Enterobacteriaceae.

(1) Laurent Poirel et al. Multiplex PCR for detection of acquired carbapenemase genes. Diagn Microbiol Infect Dis. 2011. 70, 119-23; (2) French recommendations for the prevention of « emerging extensively drug-resistant bacteria » (eXDR) cross-transmission. Lepelletier D all National Working Group.J Hosp Infect. 2015 Jul;90:186-95.(3) Emergence of plasmid mediated carbapenemase OXA-48 in a *Klebsiella pneumoniae* strain in Algeria. Aggoune N and All, 2014, jgar, Vol. 2, pp. 327-32.9.*(4)* First outbreak of OXA-48-positive carbapenem-resistant *Klebsiella pneumoniae* isolates in Constantine, Algeria. Cuzon G and all, Int J Antimicrob Agents. 2015 Dec;46(6):725-7 (5) Emergence of glycopeptide resistant *Enterococcus faecium* in Algeria: a case report Hamidi M and all.Ann Biol Clin (Paris). 2013 Jan-Feb;71(1):104-6.(6) 15ème rapport d'évaluation Janvier à Décembre 2014. Réseau Algérien de Surveillance de la Résistance des Bactéries aux Antibiotiques (AARN).