

IsDB scholars' information

- **IsDB scholar:**
 - Name : OUMAR OUCHAR MAHAMAT
 - E-mail : ouchar10@yahoo.fr
- **Home institute:**
 - Name: Centre Hospitalier Universitaire Mère et Enfant
 - Address: B.P : 6667 Ndjamenana/TCHAD
- **Host institute:**
 - Name : Université de Montpellier/institut de recherche et de développement
 - Address: 911, avenue Agropolis BP 64501 34394 Montpellier Cedex 5 France
- **IsDB scholarship :**
 - Type of IsDB scholarship : PhD
 - Year awarded : 2016
 - Year ended : 2019
- **Research work**
 - Title : Prevalence, dynamics transmission, and phenotypic and molecular characterization of extended-spectrum β -lactamase and carbapenemases producing Enterobacteriaceae in Chad
 - Summary :

The emergence and spread of antibiotic-resistant Enterobacteriaceae constitute a major public health issue worldwide. β -lactamases are the most common mechanisms of antibiotic resistance found in Enterobacteriaceae. They inactivate β -lactam antibiotics that are the most widely used drugs for bacterial infection management. Due to their wide spectrum hydrolysis, extended-spectrum β -lactamases (ESBL) and carbapenemases produced by Enterobacteriaceae (ESPL-PE and CPE) are at the origin of therapeutic impasses. Although the spread of these genes of resistance is starting to be well documented worldwide, studies on β -lactamase-producing Enterobacteriaceae remain scarce in some geographical areas. The literature search highlighted the lack of information on the genetic supports of resistance and their dynamics of transmission within human and animal in sub-Saharan Africa. To date, in Chad, the genetic characterization and transmission of antibiotic-resistant Enterobacteriaceae have never been explored. In this context, the aim of this PhD project was to study the prevalence and the transmission dynamics of ESBL-PE and CPE in human, animal and environmental compartments in Chad. We analyzed isolates collected in N'Djamena city (Chad) between January and March 2017. In humans, bacterial isolates were collected from patients with clinical infections and from volunteers

(digestive carriage), thus including two ecological niches (hospital and community). In livestock (pigs and bovines), sampling included digestive carriage isolates from three farms and three slaughterhouses. A final sampling was carried out in the aquatic environment (sewage from hospitals and slaughterhouses, water drainage canals, and the Chari River). Bacterial isolates were first identified by MALDI-TOF, and antibiotic susceptibility testing was carried out using the disc diffusion method. Genes involved in antibiotic resistance were detected by PCR and then characterized by sequencing. The *E. coli* isolates were genotyped by MLST and VNTR. The prevalence of ESBL-PE was high in human infection (48%) and fecal carriage (44%) isolates. The ESBL enzyme CTX-M-15 was predominant (97%). In addition, the genes involved in the aminoglycoside resistance (*armA*, *rmtB* and *rmtC*), quinolones resistance (*qnrB*, *qnrD*, *qnrS*, *aac(6)-Ib-cr*, *oqxAB* and *qepA*) and plasmids containing β -lactamases TEM-1 and OXA-1 were also detected. CPE prevalence was 2.5% (5/197) in human infection and 6.5% (13/200) in fecal carriage isolates. Among these five CPE clinical isolates, two carried the blaOXA-181 gene, one the blaNDM-5 gene, and two carried the both genes (blaOXA-181 and blaNDM-5). The CPE 13 fecal carriage isolates carried the blaOXA-181 gene. The blaOXA-181 gene was on an IncX3 plasmid, and blaNDM-5 and blaCTX-M-15 were located on the same IncF plasmid. This project has also highlighted the presence of ESBL-PE in livestock (10% in pigs and 2.7% in bovines), and their spread in the aquatic environment. As in humans, there is a predominance of ESBL enzyme CTX-M-15. Finally, the analysis of the genetic diversity of ESBL- and carbapenemase-producing *E. coli* and sensitive strains isolated from human, animal and environmental samples revealed a wide variety of clones. This suggests that dissemination of resistance genes is mainly related to the transfer of plasmids belonging to different incompatibility groups (IncF, IncX3, IncL/M, IncI1, IncA/C, and IncN) between genetically different strains. To conclude, this study describes for the first time the diffusion of ESBL CTX-M-15 and, OXA-181 and NDM-5 carbapenemases in Chad by horizontal transfer among humans, animals and environment. Therefore, it is urgent to implement an adapted and effective surveillance system to limit and control this dissemination.

Keywords: Enterobacteriaceae; antibiotic resistance; ESBL; carbapenemase; CTX-M-15; OXA-181; NDM-5; dynamic transmission; genetic diversity; Chad.

- Scientific significance :
- Economic and development significance for your country and IsDB member countries

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