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**LETTER TO THE EDITOR**

# First report of OXA-181 and NDM-1 from a clinical *Klebsiella pneumoniae* isolate from Nigeria

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The carbapenemase genes *bla*$_{OXA-181}$ (a variant of OXA- 48) and *bla* $_{NDM-1}$, have been extensively identified with the Indian sub-continent. Recent studies have shown the dissemination of both those genes from India, [1] to other countries. In Nigeria, not much work has been done on the molecular identification and characterization of carbapenemase genes, however their existence in the country has been es tablished by some studies. [2, 3]

The *bla*$_{OXA-181}$ gene has been also associated with other carbapenemase genes such as the NDM-1,[1] NDM-5,[4] and VIM-4 genes.[5] In Africa, the *bla*$_{OXA-181}$ gene has only been reported in Angola,[6] and South Africa.[7] It was detected also from surveillance rectal swab isolate together with the NDM-1 and VIM-2 carbapenemase genes from a patient in Canada who was previously hospitalized in Nigeria.[8] The NDM-1 gene remains the most common NDM variant, and has been detected in several African countries including Angola, Kenya, Mauritius, Egypt, Morocco and South Africa .

Here, we report a clinical isolate from Nigeria harbouring both the *bla*$_{OXA-181}$ and *bla*$_{NDM-1}$ carbapenemase genes on IncX3 and IncA/C plasmids respectively. Previously, the presence of carbapenemase genes had been established in Nigeria. [2, 3]

The isolate was recovered from the urine sample of a two year- old male patient hospitalized for seizure in the neurological department. The patient was admitted at the emergency Paediatric unit of the National Hospital Abuja, a tertiary referral centre, for fever and recurrent breathing difficulties. Clinical examination revealed a child who was febrile and tachypnoeic. A diagnosis of acute respiratory infection was made and the patient was treated with ceftriaxone and gentamicin and later with co-trimoxazole. The urine culture yielded a *Klebsiella pneumoniae* strain that was

resistant to all β-lactams including the carbapenems (MICs ≥ 12µg/mL) and aztreonam and the fluoroquinolones. The isolate was also resistant to fosfomycin, trimethoprim-sulphamethoxazole, doxycycline, tetracycline, and erythromycin and displayed intermediate susceptibility to tigecycline. It remained however susceptible to colistin and Polymyxin B. The susceptibility of the isolate to various antibiotics was performed and determined using the E-TEST method - MIC test strips ( Liofilchem® s.r.l. Roseto degli Aruzzo, Italy) for minimium inhibitory concentrations, MIC evaluation of the carbapenems – (Etrapenem ≥ 2µg/mL, Imipenem ≥ 4µg/mL, Meropenem ≥ 4µg/mL) and colistin ≥ 2µg/mL . The disk diffusion method according to the CLSI recommendation was used for the rest of the antibiotics. The E-test was interpreted according to the manufacturer's instructions while the antibiotic discs (Oxoid, Basingstoke, UK) except tigecycline were interpreted using the 2015 CLSI breakpoints for *Enterobacteriaceae*. Tigecycline zone diameter was interpreted using EUCAST interpretive criteria (Resistant= < 15, Intermediate = 15-17mm, Susceptible= ≥ 18mm).

This *Klebsiella pneumoniae* strain yielded a positive result using the RAPIDEC® Carba-NP test (BioMérieux, Marcy L'Etoile, France), a commercialized version of the Carba-NP test and a phenotypic test for the detection of any carbapenemase activity. Further processing of the isolate by PCR and gene sequencing revealed that this *K. pneumoniae* strain harboured two carbapenemase genes namely the $bla_{\text{OXA-181}}$ and the $bla_{\text{OXA-NDM-1}}$ gene. Moreover, PCR amplification revealed the presence of the *rmtC* gene coding for a 16S RNA methylase conferring high level of resistance towards aminoglycosides. MLST revealed the isolate belonged to ST 15. This ST type has been extensively reported as being associated with carbapenem-producing *Klebsiella pneumoniae*. [9]

After a series of conjugation experiments using an azide-resistant *E. coli* reference strain and imipenem (1 mg.L) as selective agents, transconjugants expressing different carbapenemase genes were identified. Then plasmids carrying the carbapenemase genes were isolated and typed using the PCR-based replicon typing, [10] showing that the $bla_{OXA-181}$ and $bla_{NDM-1}$ genes were harboured onto IncX3 and IncA/C plasmids, respectively. The $bla_{NDM-1}$ plasmid co-harboured the *rmtC* gene as described previously.

Here, we are highlighting the emergence of OXA-181 in Nigeria, and the co-production of OXA-181 and NDM-1 from a clinical *Klebsiella pneumoniae* isolate from a patient who had never travelled abroad and had no link or contact with the Indian sub-continent. However, the nature of the carbapenemases OXA-181 and NDM-1 suggests a contamination originating in the Indian subcontinent where both genes are highly prevalent. It may well be that both those carbapenemase genes have already established in Nigeria since a long time possibly causing unsuspected outbreaks both within and outside the hospital environment. This spread of OXA-181 and NDM-1 in Africa may be related to exchange of population between Africa and Asia.

This work underscores the need for clinical laboratories to be able to identify carbapenemases in developing countries. This will contribute to the implementation of effective infection control programs. The fear of the rapid spread of carbapenemase producers in Africa is real in particular in a heavily-populated country such as Nigeria.

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**Conflicts of interest**: None

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