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Short Communication

High prevalence of ESBL-producing *Klebsiella pneumoniae* in clinical samples from central Côte d'Ivoire

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ABSTRACT

Objectives: Infections caused by multidrug-resistant *Enterobacterales* pose a significant challenge to clinical patient care, particularly in resource-constrained settings where epidemiological data on antimicrobial resistance are scarce. The aim of this study was to determine the prevalence of extended spectrum beta-lactamase-(ESBL)-producing *Klebsiella pneumoniae* among clinical samples from a teaching hospital in Bouaké, central Côte d'Ivoire.

Methods: Clinical specimens were collected from sterile and non-sterile body sites and were subjected to microbiological diagnostics (April 2016-June 2017). The antimicrobial susceptibility patterns of *K. pneumoniae* were analysed using automated resistance testing and double-disk diffusion to test for ESBL production. Multiplex PCR was carried out to determine the presence of the resistance-conferring genes $bla_{\text{CTX-M}}$, bla_{SHV} and bla_{TEM}.

Results: A total of 107 isolates were included, most of which were obtained from bloodstream (39%; n = 42) and urinary tract infections (39%; n = 42). Among all *K. pneumoniae* isolates, 84% (n = 90) were ESBL producers, many of which were also not susceptible to sulfonamides (99%), quinolones (81%) and aminoglycosides (79%). The majority of ESBL-producing strains harboured all three investigated *bla* genes.

Conclusion: The high prevalence of ESBL-producing *K. pneumoniae* in clinical isolates from Côte d'Ivoire calls for revised empirical treatment regimens in critically ill patients with suspected Gram-negative infections, and the establishment of antimicrobial resistance surveillance systems.

Introduction

The spread of multidrug-resistant bacteria has become a public health concern on a global scale and particularly affects low- and middle-income countries (Ndihokubwayo et al., 2013; O'Neill, 2016; Okeke et al., 2005; World Health Organization, 2011). However, epidemiological data on multi-resistant organisms in sub-Saharan Africa are scarce (Storberg, 2014). A recent systematic review elucidated that the lack of data on the occurrence of multi-resistant Gram-negative bacteria (e.g. *Klebsiella pneumoniae*) is greatest in West Africa (Workneh et al., 2017). In an attempt to start filling this epidemiological gap, we conducted a hospital-based study on the prevalence of *K. pneumoniae* with extended spectrum beta-lactamases (ESBL) among clinical specimens collected at the University Teaching Hospital Bouaké (UTHB) in Côte d'Ivoire.

Methods

A hospital-based study was conducted between April 2016 and June 2017 at UTHB in Bouaké, central Côte d'Ivoire, the country's only University hospital outside the economic capital Abidjan.

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Table 1
Epidemiological and clinical data of patients with detection of *Klebsiella pneumoniae* in clinical specimens at the University Teaching Hospital in Bouaké, central Côte d'Ivoire, 2016–2017.

Patient characteristics	Total (%)
Number of patients	107 (100)
Median age in years (range)	34 (2–84)
Sex	
Female	64 (59.8)
Male	43 (40.2)
Ward of admission	
Paediatrics	31 (29.0)
Internal medicine	26 (24.3)
Intensive care unit	15 (14.0)
Urology	11 (10.3)
Traumatology	7 (6.5)
Neurology	5 (4.7)
General surgery	3 (2.8)
Neurosurgery	2 (1.9)
Other	7 (6.5)
Biological specimen collected	
Blood	42 (39.3)
Urine	42 (39.3)
Swabs (wound or pus)	15 (14.0)
Pleural effusion	3 (2.8)
Bronchial secretion	2 (1.9)
Cerebrospinal fluid	1 (0.9)
Joint aspirate	1 (0.9)
Other	1 (0.9)

Clinical specimens were collected as part of the routine diagnostics from inpatients and comprised specimens from sterile (e.g. blood cultures) and non-sterile body sites (e.g. wound swabs). The decision to send samples for microbiological analysis was based on the judgement of the attending physician. No specific exclusion/inclusion criteria were applied.

Clinical samples were processed at the local microbiology laboratory using routine diagnostic methods (i.e. bacterial culture on blood agar and MacConkey agar plates). Gram-negative isolates were provisionally identified as *K. pneumoniae* based on colony morphology and enzymatic tests (API NE, BioMérieux; Marcy L'Étoile, France). Isolates were subsequently transferred to Homburg, Germany for confirmatory testing using matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry (Maldi Biotyper, Bruker Daltonics; Bremen, Germany). *K. pneumoniae* strains were subjected to antibiotic susceptibility testing (VITEK®2, bioMérieux; Marcy L'Étoile, France). Resistance patterns were interpreted according to breakpoints put forth by the European Committee on Antimicrobial Susceptibility Testing (EUCAST; version 7.1). ESBL-producing *K. pneumoniae* were phaenotypically confirmed by double disk diffusion test containing cefotaxime or ceftazidime with and without clavulanic acid (Mast Diagnostics; Bootle, United Kingdom). Additionally, genotypic detection of different beta-lactamase encoding genes was carried out in Münster, Germany (Monstein et al., 2007).

Results

During the study period, we included 107 patients with *K. pneumoniae* isolates detected in clinical specimens. There were more female patients and most samples were obtained from the paediatric ward (29%), followed by internal medicine (24%) and the hospital's interdisciplinary intensive care unit (14%). The majority of isolates stemmed from bloodstream infections (39%) and urine samples (39%; Table 1).

Automated susceptibility tests and double-disk diffusion showed a 100% concordance in determining ESBL phenotypes, and confirmed 90 of the 107 isolates (84%) as ESBL-producing *K.*

Table 2
Antimicrobial susceptibility patterns of 107 *K. pneumoniae* isolates obtained from human infections at the University Teaching Hospital in Bouaké, central Côte d'Ivoire, 2016–2017. ESBL-producing isolates are stratified by the distribution of *bla* genes.

Characteristics of *K. pneumoniae* isolates	Number (%)	Presence of *bla* genes	Antimicrobial susceptibility testing (R, resistant; I, intermediate; S, susceptible)								
			Ampicillin/ Sulbactam	Piperacillin/ tazobactam	Cefuroxime	Cefotaxime	Ceftazidime	Meropenem	Ciprofloxacin	Gentamicin	Sulfamethoxazol/ trimethoprim
ESBL production	90 (84%)		R: 90 (100%) I: - S: -	R: 28 (31%) I: 51 (57%) S: 11 (12%)	R: 90 (100%) I: - S: -	R: 90 (100%) I: - S: -	R: 77 (86%) I: 12 (13%) S: 1 (1%)	R: - I: - S: 90 (100%)	R: 56 (62%) I: 17 (19%) S: 17 (19%)	R: 71 (79%) I: - S: 19 (21%)	R: 89 (99%) I: - S: 1 (1%)
	1	bla_{SHV}	R: 1	I: 1	R: 1	R: 1	R: 1	S: 1	R: 1	R: 1	R: 1
	1	bla_{CTX-M}	R: 1	I: 1	R: 1	R: 1	R: 1	S: 1	R: 1	R: 1	R: 1
	2	bla_{TEM}	R: 2	R: 2	R: 2	R: 2	R: 1; S: 1	S: 2	R: 2	R: 1; S: 1	R: 2
	7	bla_{SHV} +bla_{CTX-M}	R: 7	R: 2; I: 1; S: 4	R: 7	R: 7	R: 7	S: 7	R: 3; I: 1; S: 3	R: 4; S: 3	R: 6; S: 1
	12	bla_{CTX-M} + bla_{TEM}	R: 12	R: 5; I: 5; S: 2	R: 12	R: 12	R: 12	S: 12	R: 10; S: 2	R: 9; S: 3	R: 12
	64	bla_{SHV} + bla_{CTX-M} + bla_{TEM}	R: 64	R: 17; I: 43; S: 4	R: 64	R: 64	R: 52; I: 12	S: 64	R: 37; I: 16; S: 11	R: 52; S: 12	R: 64
	3	Negative for bla_{SHV}/ bla_{CTX-M}/ bla_{TEM}	R: 3	R: 2; I: 1	R: 3	R: 3	R: 3	S: 3	R: 2; S: 1	R: 3	R: 3
No ESBL production	17 (16%)	–	R: 4 (24%) I: 11 (65%) S: 2 (12%)	R: 1 (6%) I: - S: 16 (94%)	R: - I: - S: 17 (100%)	R: - I: - S: 17 (100%)	R: - I: - S: 17 (100%)	R: - I: - S: 17 (100%)	R: 1 (6%) I: 1 (6%) S: 15 (88%)	R: 1 (6%) I: - S: 16 (94%)	R: 3 (18%) I: - S: 14 (82%)
Total	107 (100%)		R: 94 (88%) I: 11 (10%) S: 2 (2%)	R: 28 (27%) I: 51 (48%) S: 27 (25%)	R: 90 (84%) I: - S: 17 (16%)	R: 90 (84%) I: - S: 17 (16%)	R: 77 (72%) I: 12 (11%) S: 18 (17%)	R: - I: - S: 107 (100%)	R: 57 (53%) I: 18 (17%) S: 32 (30%)	R: 72 (67%) I: - S: 35 (33%)	R: 92 (86%) I: - S: 15 (14%)

pneumoniae. Multiplex PCR elucidated that 71% of these strains concomitantly harboured the beta-lactamase-encoding genes bla_{SHV}, $bla_{CTX\text{-}M}$ and bla_{TEM} (Table 2).

Among all detected *K. pneumoniae* strains, the ESBL prevalence was 94% in samples stemming from paediatric patients (<18 years) as opposed to 79% in adults. Phaenotypic resistance to third-generation cephalosporins (i.e. cefotaxime) was observed in 84% of all isolates, whereas no resistance to carbapenems was detected. Non-susceptibility to sulfamethoxazole/trimethoprim (99%), ciprofloxacin (81%) and gentamicin (79%) was common in ESBL-producing isolates, whereas these antibiotics remained active against most *K. pneumoniae* strains with no ESBL production.

Discussion

We found a very high prevalence of ESBL-producing isolates (84%) among all *K. pneumoniae* strains detected in clinical specimens from a teaching hospital in Côte d'Ivoire, with paediatric patients being most frequently affected. The ESBL prevalence reported here is much higher than previously observed for *K. pneumoniae* in human samples from south Côte d'Ivoire (Tahou et al., 2017) and from neighbouring Burkina Faso (Kpoda et al., 2018).

Third-generation cephalosporines are widely used as first-line antibiotics in the empirical treatment of many infections in sub-Saharan Africa. Indeed, these drugs were the most commonly administered antibiotics in patients with bloodstream infections at UTHB, followed by penicillin derivatives, all of which are hydrolysed by ESBL (Akoua-Koffi et al., 2015). Given the high prevalence of ESBL-producing *K. pneumoniae* detected in our present study, the empirical use of third-generation cephalosporins in critically ill patients needs to be urgently revised. Additionally, further studies are needed to assess the impact of antibiotic self-medication prior to hospitalisation on the spread of resistance, as antibiotics are easily accessible 'over-the-counter' and without prescription in parts of Côte d'Ivoire (Hounsa et al., 2010).

Limitations of this study include the relatively small study population and the lack of additional clinical data (e.g. data on prior admission to hospital or previous antibiotic treatment) that might help to identify patients at particular risk of ESBL carriage. Moreover, further characterisation of ESBL subtypes was not feasible and we did not perform environmental sampling, which might have been useful to detect potential nosocomial transmission patterns.

Our findings call for an urgent implementation of strategies to tackle antimicrobial resistance in Côte d'Ivoire. Indeed, the lack of appropriate microbiological testing facilities (Okeke, 2006) and the absence of antimicrobial stewardship initiatives (Hamilton and Bugg, 2018) have been identified as important factors that are associated with a suboptimal management of severe infections in sub-Saharan Africa. Hence, we propose a bundle of measures, which comprise (i) improved surveillance systems to monitor emerging resistance patterns (e.g., via antibiotic stewardship initiatives); (ii) well-equipped microbiology laboratories to obtain reliable test results; and (iii) improved access to antibiotics with efficacy against ESBL-producing isolates (e.g. carbapenems) for the empirical treatment of severely ill patients in Côte d'Ivoire.

Conflict of interest statement

All authors do not have any conflicts of interest to declare.

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Ethical approval

The study was approved by the medical and scientific directorate at UTHB on behalf of the Ministry of Public Health in Côte d'Ivoire (reference no.: 41-MSHP/CHU-B/DG/DMS/ONAR/16).

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