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ABSTRACT



04821 The evolution of carbapenem resistance determinants and major

epidemiological lineages among carbapenem-resistant *Acinetobacter baumannii*

isolates in Germany, 2010-2019

03. Bacterial susceptibility & resistance

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Background

Acinetobacter baumannii is a major pathogen causing healthcare-associated infections, especially in intensive care units (ICU). While carbapenems play an important role in the treatment of *A. baumannii* infections, the species can develop carbapenem resistance due to overexpression of the intrinsic class D β -lactamase gene *bla*_{OXA-51-like} or presence of acquired genes including *bla*_{OXA-23-like}, *bla*_{OXA-40-like} and *bla*_{OXA-58-like}. The objectives of this study were i) to evaluate the occurrence of carbapenem resistance determinants among *A. baumannii* isolates collected during four multicentre surveillance studies conducted by the Paul-Ehrlich-Society between 2010 and 2019, and ii) to investigate the molecular epidemiology of these isolates.

Methods

Isolates were collected prospectively from hospitalised patients at 17 medical centres in Germany, in each case over a three-month-period in the years 2010, 2013, 2016 and 2019. Verification of species identification and susceptibility testing were performed in a reference laboratory. MICs were determined by broth microdilution (ISO-standard) and interpreted by EUCAST breakpoints (v.11.0). The prevalence of

*bla*_{OXA} genes was investigated by oxacillinase (OXA)-multiplex PCR and whole-genome sequencing. The molecular epidemiology was examined by repetitive sequence-based PCR (rep-PCR; DiversiLab) and core-genome MLST.

Results

Overall, 302 *A. baumannii* isolates were collected, including 72 ICU isolates and 230 non-ICU isolates. Resistance to imipenem and/or meropenem was detected in 58 isolates (Table 1). The proportion of resistant isolates evolved from 16/75 (21.3%) in 2010 to 20/60 (33.3%) in 2013 and then decreased to 13/94 (13.8%) in 2016 and 9/73 (12.3%) in 2019 (chi-squared trend analysis, $p < 0.05$). Forty-six carbapenem-resistant isolates (79.3%) were associated with the clonal lineage IC 2 and five (8.6%) with IC 1 (Table 2). The majority of resistant isolates (87.9%) encoded *bla*_{OXA-23}-like (Table 3). Other carbapenem-resistance determinants detected were OXA-40-like ($n=1$), OXA-58-like ($n=3$), overexpression of OXA-51-like ($n=1$) and NDM-1 ($n=2$).

Conclusions

This nationwide study found a pooled rate of non-susceptibility to carbapenems in *A. baumannii* of 19.2% (95%-CI: 14.8-23.6%) in the period 2010-2019. Interestingly, a decrease in carbapenem-resistant isolates was detected from 2013 onwards, which seems to indicate a reduction of carbapenem resistance in this species in Germany.

Table 1

Table 1. Geographical distribution of the *A. baumannii* isolates ($n=302$) and number of carbapenem-resistant (CR) isolates by year of isolation

Centre	Year of isolation								No. of CR isolates 2010-2019
	2010		2013		2016		2019		
	No. collected	No. CR	No. collected	No. CR	No. collected	No. CR	No. collected	No. CR	
306	5	-	2	-	2	-	2	-	-
309	1	-	2	1	6	-	2	-	1
312	10	-	1	-	9	-	4	2	2
317	1	-	-	-	2	1	1	-	1
318	2	1	8	6	2	-	7	2	9
319	6	-	4	-	6	3	9	-	3
321	1	-	4	-	4	-	-	-	-
322	1	-	3	-	10	1	10	-	1
323	5	1	1	1	6	3	4	-	5
324	6	1	5	-	5	2	4	-	3
325	11	3	8	3	5	1	6	-	7
326	7	2	6	5	5	-	7	2	9
352	1	1	5	-	9	-	7	1	2
353	11	5	4	3	2	1	4	2	11
355	-	-	-	-	12	-	2	-	-
356	5	1	4	-	2	-	3	-	1
357	2	1	3	1	7	1	1	-	3
Total	75	16	60	20	94	13	73	9	58
% CR		21.3		33.3		13.8		12.3	19.2

Table 2

Table 2: International clonal (IC) lineages associated with carbapenem-resistant *A. baumannii* (n=58) by year of isolation

Clonal lineage	Year of isolation				Total
	2010	2013	2016	2019	
IC-1		1	4		5
IC-2	14	18	6	8	46
IC-4	1				1
IC-7			1		1
No IC	1	1	2	1	5
Total	16	20	13	9	58

Table 3

Table 3: Prevalence of acquired CP genes by year of isolation

Clonal lineage	CP gene	Year of isolation				Total
		2010	2013	2016	2019	
IC-1	OXA-23-like		1	4		5
IC-2	OXA-23-like	13	16	6	8	43
	OXA-40-like		1			1
IC-4	OXA-58-like	1	1			2
	Overexpression of OXA-51-like	1				1
IC-7	OXA 23-like			1		1
No IC	OXA-23-like	1		1		2
	NDM-1		1	1		2
	OXA-58-like				1	1
Total		16	20	13	9	58