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Bacteriology | New-Data Letter

Acinetobacter baumannii international clone 2 co-producing OXA-23, NDM-1, and ArmA emerging in South America

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Acinetobacter baumannii is a leading cause of healthcare-associated infections worldwide. The clinical significance of *A. baumannii* lies in its ability to acquire multiple resistance determinants resulting in difficult-to-treat infections (1). In this regard, carbapenem-resistant *A. baumannii* are in the top position of "the WHO priority pathogens", for which novel antibiotics are needed (2). In South America, the endemic status of carbapenem-resistant *A. baumannii* has been associated with the production of OXA-23 carbapenemases by international clones IC1 (clonal complex, CC1), IC4 (CC15), IC5 (CC79), and IC7 (CC25) (1, 3, 4). More recently, IC2 (sequence type, ST2) has been detected in Argentina, Brazil, Ecuador, Paraguay, Peru, and Venezuela (1, 5–7). In this study, as part of the Grand Challenges Explorations: New Approaches to Characterize the Global Burden of Antimicrobial Resistance Program, we report the emergence and genomic characteristics of an extensively drug-resistant (XDR) lineage of *A. baumannii* (8), subclone (ST2:KL9:OCL1) of the parental epidemic international clone 2, exhibiting an evolutionary bacterial resistance trend toward the co-production of ArmA methyltransferase and OXA-23 plus NDM-1 carbapenemases, along with the acquisition of colistin resistance.

Between April and September 2022, during a hospital outbreak of *A. baumannii* infections, with 21 fatal outcomes among 28 patients admitted to an intensive care unit (ICU) and hospital ward of a teaching hospital in Southern Brazil, a representative XDR strain (Ab375) isolated from a bloodstream infection of an ICU patient who died due to cardiopulmonary arrest was investigated in depth. Bacterial identification (Bruker Biotyper matrix-assisted laser desorption/ionization-time of flight mass spectrometry, MALDI-TOF MS), antimicrobial susceptibility, and Illumina next-generation sequencing were performed to extract clinically relevant information, whereas publicly available *A. baumannii* ST2 genomes (https://www.ncbi.nlm.nih.gov/genome), and capsule (K) and outer core (OC) loci (https://kaptive-web.erc.monash.edu/) profiling were used for comparative phylogenomic analysis and identification of *A. baumannii* subclones. The genetic context of clinically relevant genes was investigated using Geneious Prime R10 (Fig. S1), nucleotide BLAST (https://blast.ncbi.nlm.nih.gov/Blast.cgi), and ISFinder (https://isfinder.biotoul.fr). Detailed material and method information is provided in the supplementary text.

The Ab375 strain displayed resistance to β-lactams, aminoglycosides, fluoroquinolones, trimethoprim-sulfamethoxazole, and colistin, remaining susceptible to minocycline and cefiderocol alone. Sequence analysis revealed a wide resistome with genes encoding carbapenemases (bla_{OXA-23} and bla_{NDM-1}) and aminoglycoside-modifying enzymes (*aadA1*, *aac(6')-Ib3*, *aph(3")-Ib*, *aph(3')-Ia*, *aph(3')-VI*, *aph(6)-Id*), as well as the 16S rRNA methyltransferase *armA* gene that confers pan-aminoglycoside resistance. In

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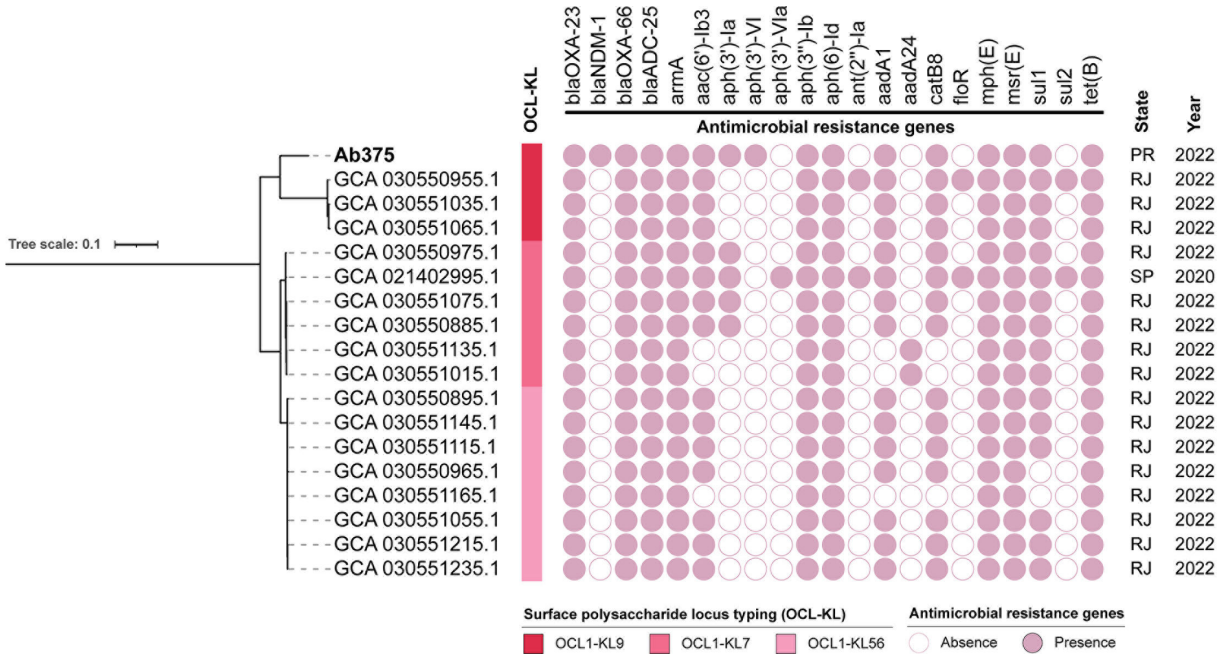

FIG 1 Phylogenomic relationship, resistome, and surface polysaccharide locus typing of carbapenem-resistant *A. baumannii* ST2 strains from Brazil.

addition, gene mutations related to colistin and fluoroquinolone resistance (9, 10), and virulence genes of seven groups (adherence, biofilm formation, immune evasion, iron uptake, quorum sensing, cell invasion, and stress adaptation) were also detected (Table S1).

A. baumannii Ab375 belonged to Pasteur MLST-ST2 (IC2), a global highly pathogenic clone associated with strong biofilm formation and high serum survival (11). Phylogenomics clustered Ab375 along with three *A. baumannii* ST2 strains isolated in 2022, from inpatients in Rio de Janeiro (Fig. 1; Table S2). Noteworthy, this cluster displayed an identical outer core (OCL1) and capsular polysaccharide (KL9) locus, confirming the emergence of subclone KL9:OCL1 within the IC2 circulating in South America (Table S3).

In summary, we report a novel epidemiological and resistance event of medical and public health interest worldwide, alerting the scientific community that genomic monitoring of critical priority lineages of *A. baumannii* is urgent to prevent their further spread.

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ADDITIONAL FILES

The following material is available online.

Supplemental Material

Figure S1 (AAC00298-24-S0001.docx). Schematic representation of the genetic environment of antimicrobial resistance genes carried by *Acinetobacter baumannii* Ab375 strain isolated in Paraná, Brazil.
Supplemental text (AAC00298-24-S0002.docx). Detailed material and method information.
Table S1 (AAC00298-24-S0003.docx). Clinical, microbiological, and genomic characteristics of *A. baumannii* IC2 Ab375 strain.

Table S2 (AAC00298-24-S0004.xlsx). Matrix containing the pairwise number of SNP differences between all pairs of *Acinetobacter baumannii* IC2 lineages from Brazil (2020-2022).

Table S3 (AAC00298-24-S0005.xlsx). Epidemiological and clinically relevant genomic data of *Acinetobacter baumannii* IC2 lineages from South America (NCBI, PubMLST, Kaptive, and Resfinder v.4.4.2).

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