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Practice points

Carbapenem-resistant Gram-negative bloodstream infections in critically ill children: outcome and risk factors in a tertiary teaching hospital in South America

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Gram-negative bacteria are a major cause of healthcare-acquired infections in developing countries [1–3]. The emergence of carbapenem resistance is a global public health issue given the scarcity of treatment options, and high mortality rates and hospital costs [4,5]. Children are less affected by carbapenem resistance than adults, but they have fewer treatment options, and mortality rates, despite being lower than in adults, may be as high as 50% [5,6].

This study reviewed all healthcare-acquired bloodstream infections (HA-BSIs) caused by Gram-negative micro-organisms in the paediatric intensive care unit (PICU) of Santa Casa de São Paulo — a tertiary teaching hospital in Sao Paulo, Brazil — between January 2012 and December 2016. As some patients had more than one HA-BSI during their stay in the PICU, only the first episode was included in this study. Patients were divided into two groups according to carbapenem resistance, and statistical analysis was performed to compare outcomes and previous clinical conditions.

In total, there were 62 Gram-negative HA-BSIs during the study period. Of these, 96.7% were central line associated, and 19 (30.6%) were caused by a carbapenem-resistant (CR) micro-organism.

Table I shows data for demographic and clinical conditions prior to HA-BSI in both groups.

Patients in the CR group had undergone more surgery prior to HA-BSI than patients in the carbapenem-susceptible (CS) group (P=0.02). The most common surgical procedure in both groups was cardiothoracic surgery (44.5% and 60% of all surgeries in the CR and CS groups, respectively).

The use of any broad-spectrum antibiotic and a treatment duration exceeding 14 days did not differ between groups, but the use of carbapenems specifically in the past 30 days was significantly higher in the CR group (P=0.005).

No difference in previous colonization by a CR Gram-negative micro-organism was found between the groups, but the data were limited given the lack of routine surveillance due to financial constraints at the study institution during the study period.

Acinetobacter baumannii, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were the most frequently isolated bacteria in both groups, accounting for 70% of all positive cultures. Carbapenem resistance was found in 50%, 42.8% and 22.3% of these isolates, respectively. Other bacteria found in this study included one CR *Burkholderia cepacea*

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Table I
Characteristics of patients with carbapenem-resistant Gram-negative (CRGN) and carbapenem-susceptible Gram-negative (CSGN) healthcare-associated bloodstream infections (HA-BSIs)

	CRGN	CSGN	*P*-value
Age [months; median (IQR)]	19.2 (8.2—79.3)	8.5 (4.0—23.6)	0.16
Female (*N*, %)	4 (21%)	14 (32.5%)	0.54
Underlying conditions (*N*, %)	17 (89.4%)	32 (74.4%)	0.31
Previous known CRGN colonization	7 (36.8%)	10 (23.2%)	0.12
Hospital length of stay prior to HA-BSI [days; mean (SD)]	28.8 (5.11)	28.6 (3.62)	0.96
PICU length of stay prior to HA-BSI [days; mean (SD)]	24.8 (5.33)	16.6 (2.19)	0.16
No. of CVC days prior to HA-BSI [days; mean (SD)]	21.3 (3.06)	21.8 (2.58)	0.90
Use of parenteral nutrition (*N*, %)	4 (21.0%)	5 (11.6%)	0.43
Surgery prior to HA-BSI in the same hospitalization (*N*, %)	9 (47.3%)	10 (23.2%)	0.02
Use of antibiotics in the previous 30 days (*N*, %)	17 (89.4%)	31 (72.0%)	0.16
Duration of previous antibiotic course over 14 days (*N*, %)	10 (52.6%)	12 (27.9%)	0.22
Use of carbapenems in the previous 30 days (*N*, %)	10 (52.6%)	7 (16.2%)	0.005
Previous hospitalization in the last 12 months (*N*, %)	6 (31.5%)	16 (37.2%)	0.76
Previous HAI during the same hospitalization (*N*, %)	7 (36.8%)	11 (25.5%)	0.53

IQR, interquartile range; SD, standard deviation; CVC, central venous catheter; HAI, healthcare-acquired infection; PICU, paediatric intensive care unit.

isolate, and CS *Citrobacter* spp., *Enterobacter* spp. and *Serratia* spp.

A previous study at the same institution found no evidence of carbapenem resistance in Enterobacteriaceae from 2001 to 2003, meaning that the prevalence of carbapenem resistance in *K. pneumoniae* HA-BSI has risen from 0 to 42.8% in 10 years [7].

Only 15.7% of patients in the CR group received appropriate initial antimicrobial therapy. This is an important finding, given that at least 18% of all HA-BSIs in the study PICU were caused by CR Gram-negative bacteria [8]. There was no significant difference in either PICU or hospital length of stay between the groups ($P=0.23$ and $P=0.12$, respectively), but mortality was significantly higher in the CR group (52.6% vs 4.65%, $P\leq0.0001$).

This study is limited by the small sample size and the fact that it was based at a single centre. However, the results add to understanding of the characteristics of HA-BSIs with CR Gram-negative bacteria in children in developing countries, and highlight the need for antibiotic stewardship campaigns focusing on the use of carbapenems.

Conflict of interest statement
None declared.

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