Carbapenem-resistant gram-negative pathogens in Brazil: Analysis from patients in a laboratory network

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Introduction

- Treatment of gram-negative infections has become increasingly complicated by the emergence of carbapenem-resistant *Enterobacterales*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*[1-3]

- Such infections impose important clinical and economic impacts.[4-6] In Brazil, data on economic impact are scarce, but a study estimated that each hospitalized patient from a Brazilian state (Mato Grosso do Sul) with carbapenem-resistant strains spent a median of US$ 3.174,87 in the treatment, (equivalent to about 15 minimum Brazilian wages), creating an undue economic burden with a high cost of hospitalization[6]

- Despite this impact, there is still a lack of robust national data regarding the occurrence of carbapenem-resistant gram-negative pathogens in Brazil

Objective

- This study aims to determine the frequency of *Enterobacterales* and *P. aeruginosa* in Brazil from 2018-2020, and their carbapenem-resistance rates

Methods

- A cross-sectional study was conducted using a database from a private laboratory network, between January 2018 and June 2020

- Data from blood, urine, and respiratory tract samples attending the study criteria were considered in this analysis. Individuals were included if the following inclusion criteria were met: non-consecutive isolates collected from each site of infection; *Enterobacterales* and *P. aeruginosa* isolates and isolates from patients ≥18 years old. Also, were included isolates from inpatients only. **Figure 1** shows the study inclusion flowchart

- Antimicrobial susceptibility for samples from intensive care unit was determined by broth microdilution, and by disk diffusion for other samples. Susceptibility was interpreted using BRCAST/EUCAST according to the year of the sample collection. Carbapenem resistance was defined as resistance to imipenem or meropenem for *P. aeruginosa*, and resistance to ertapenem for *Enterobacterales*

- Data were analyzed in a descriptive approach through measures of frequency. Data transformation and analysis were performed in Knime, version 3.53, and R, version 4.1.2

Figure 1. Patients' inclusion flowchart
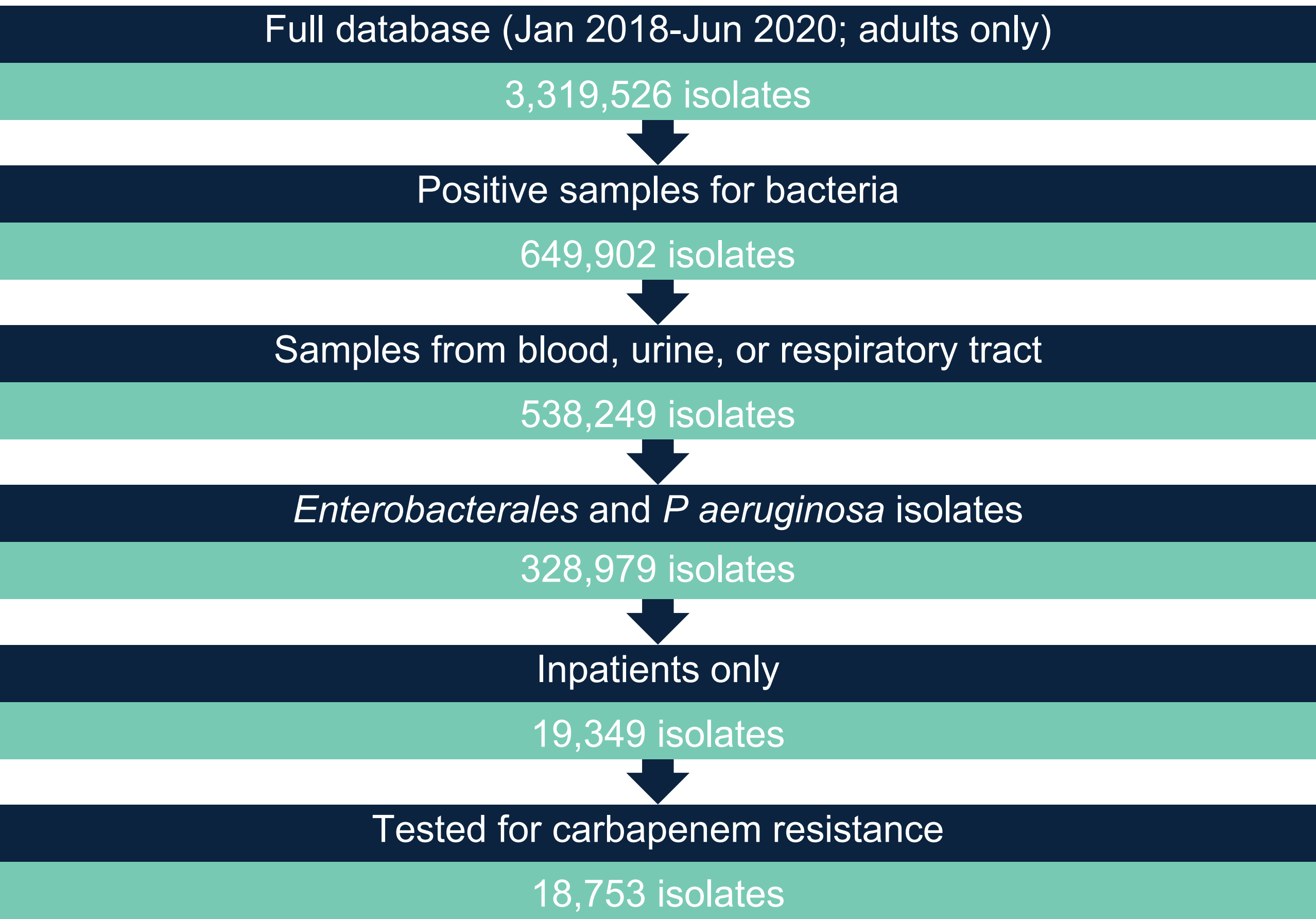
Results

- The analyzed sample consists of 18,753 isolates from 17,062 patients. **Table 1** shows general characteristics of the sample

  – Patients were mostly female (59%) with almost 65% of them with more than 63 years old (mean: 70; SD: 18)

  – Isolates were collected from 5 of 26 Brazilian states

  – Ninety-seven percent of the patients were from the south and southeast regions of Brazil (22% and 75%, respectively)

Table 1. General characteristics of the study sample

Variables	n	%
Patients (N)	17,062	100.0
Sex		
Female	10,035	58.8
Male	7,027	41.2
Age (SD)	70	58.8
Age groups		
18-33 years	926	5.4
34-50 years	1,720	10.1
51-66 years	3,397	19.9
67-83 years	6,599	38.7
84-100 years	4,384	25.7
100+ years	36	0.2
Region		
Southeast	12,705	74.5
South	3,795	22.2
Midwest	445	2.6
North	117	0.7

SD: standard deviation.

- **Table 2** shows the resistance pattern according to different sociodemographic characteristics

  – A total of 18,753 samples were included in the analysis, 5,975 (31.9%) *P. aeruginosa*, 11,169 (59.5%) *non-Morganellaceae Enterobacterales*, and 1,609 (8.6%) *Morganellaceae* (*Morganella*, *Proteus* and *Providencia spp*)

  – Almost 50% of the *P. aeruginosa* samples were carbapenem-resistant, while only 6% and 2% of the *non-Morganellaceae Enterobacterales* and *Morganellaceae*, respectively, showed the same trait

  – Carbapenem-resistance pattern was more common in the midwest region for n*on-Morganellaceae Enterobacterales* and *Morganellaceae* (22% and 8%, respectively), while the northeast region showed higher values for *P. aeruginosa* (52%)

Table 2. Carbapenem-resistance according to demographic characteristics

	non-Morganellaceae Enterobacterales	P. aeruginosa	Morganellaceae
	n resistance/N total (%)		
Resistance	**654/11,169 (5.9)**	**2,671/5,975 (44.7)**	**32/1,609 (2)**
Resistance by sex			
Female	282/7,485 (3.8)	926/2,497 (37.1)	13/904 (1.4)
Male	372/3,684 (10.1)	1,745/3,478 (50.2)	19/705 (2.7)
Resistance by age group			
18-33 years	37/689 (5.4)	145/292 (49.7)	0/33 (0)
34-50 years	67/1,316 (5.1)	216/451 (47.9)	1/128 (0.8)
51-66 years	140/2,263 (6.2)	506/1,156 (43.8)	11/323 (3.4)
67-83 years	250/4,184 (6)	1,181/2,461 (48)	14/657 (2.1)
84-100 years	160/2,692 (5.9)	621/1,604 (38.7)	6/464 (1.3)
101+ years	0/25 (0)	2/11 (18.2)	0/4 (0)
Region			
Southeast	313/7,884 (4)	2,043/4,364 (46.8)	19/1,190 (1.6)
South	200/2,602 (7.7)	541/1,406 (38.5)	4/279 (1.4)
Midwest	121/546 (22.2)	39/112 (34.8)	9/114 (7.9)
Northeast	20/137 (14.6)	48/93 (51.6)	0/26 (0)

- In **Table 3**, information related to resistance pattern according to the collected material is shown. Respiratory tract isolates showed higher values of carbapenem-resistance pattern across all specimens (55%, 14%, and 4% for *P. aeruginosa*, *non-Morganellaceae Enterobacterales*, and *Morganellaceae*, respectively)

Table 3. Carbapenem-resistance according to material

	non-Morganellaceae Enterobacterales	P. aeruginosa	Morganellaceae
	n resistance/N total (%)		
Isolate material			
Respiratory tract	170/1,215 (14)	1,738/3,187 (54.5)	16/383 (4.2)
Blood	192/2,329 (8.2)	306/892 (34.3)	4/253 (1.6)
Urine	292/7,625 (3.8)	627/1,896 (33.1)	12/973 (1.2)

- Finally, carbapenem-resistance pattern was assessed according to the species within each group (**Table 4**). We highlight that 54% of *K. pneumoniae* samples showed such pattern. The highest frequency of resistance was observed in the *non-Morganellaceae Enterobacterales* group

Table 4. Carbapenem-resistance according to species within each group

	non-Morganellaceae Enterobacterales[1]	P. aeruginosa	Morganellaceae
	n resistance/N total (%)		
Serratia marcescens	73/991 (7.4)	-	-
Escherichia coli	115/8,302 (1.4)	-	-
Enterobacter cloacae	331/1,363 (24.3)	-	-
Citrobacter freundii	10/281 (3.6)	-	-
Klebsiella pneumoniae	125/232 (53.9)	-	-
Pseudomonas aeruginosa	-	2,671/5,975 (44.7)	-
Morganella morganii	-	-	7/343 (2)
Proteus mirabilis	-	-	12/1,135 (1.1)
Providencia rettgeri	-	-	3/30 (10)
Providencia stuartii	-	-	10/101 (9.9)

Conclusion

- We observed a high prevalence of carbapenem-resistant gram-negative pathogens among hospitalized patients in Brazil

- Carbapenem-resistance rates are lower in *non-Morganellaceae Enterobacterales* due to the high frequency of *E. coli* in the isolates. However, in the individual analysis of *K. pneumoniae*, we found a high incidence of resistance to carbapenems

- These data should reinforce the urgency of having strategies to fight against antimicrobial resistance

References

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