Global point prevalence survey of antimicrobial consumption in Brazilian hospitals

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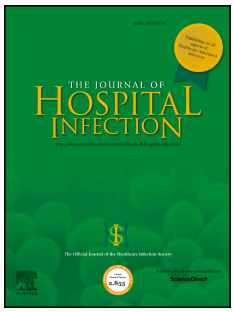

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Global Point Prevalence Survey (Global-PPS) of Antimicrobial Consumption in Brazilian Hospitals

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Abstract

Background: The inappropriate use of antimicrobials and increased rates of antimicrobial resistance is a challenge all over the world. Although antibiotic stewardship is recommended by the Brazilian government, data regarding antibiotic use in Brazilian hospitals are scarce.

Aim: The aim of this study was to conduct a point prevalence survey of antimicrobial use in 18 Brazilian hospitals.

Methods: Eighteen Brazilian hospitals conducted the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) in 2017.

The study enrolled inpatients on antimicrobials. Data collection included details on the antimicrobial prescriptions. A web-based program was used for data-entry, validation and reporting. The Global-PPS was developed by the University of Antwerp and bioMérieux provided funding support.

Findings: We evaluated 1801 patients, of which 941 (52.2%) were on antimicrobials. Four hundred (42.5%) patients were given at least two antimicrobials. Out of the 1317 antibacterials for systemic use, 514 (39%) were prescribed for community-acquired infections, 533 (40.5%) for healthcare-associated infections and 248 (18.8%) for prophylactic use. The most frequently used antimicrobials were ceftriaxone (12.8%), meropenem (12.3%) and vancomycin (10.3%). Pneumonia or lower tract respiratory infection was the the most common site of infection (29.2%). In general, antimicrobials were given mainly parenterally (91%) and empirically (81.2%).

Conclusions: We observed a high prevalence of antibiotic use in the 18 Brazilian hospitals. The antibiotics were prescribed mainly empirically. Intravenous broad-spectrum antibiotics were the most frequent antimicrobials used, showing that reinforcement of de-escalation strategy is needed. The Global-PPS data can be very useful for monitoring stewardship programmes and intervention.

Introduction

The inappropriate use of antibiotics and increased rates of antimicrobial resistance are challenges all over the world, which have been associated with increased morbidity, mortality and health care costs.[1] Although the antimicrobial

resistance rates vary widely in South America, a particular concern is the trend for increasing antimicrobial resistance in Gram-negative bacteria reported from many countries.[2-3]

Thus, an important approach to contain the emergence of antimicrobial resistance and optimize antimicrobial usage, ensuring appropriate antimicrobial use, relies on programs called antimicrobial stewardship programs (ASP).[4] The Centers for Disease Control and Prevention (CDC) reports that 30% of all antibiotics prescribed in the USA are either unnecessary or inappropriate.[5] Data about quantity and quality of antimicrobial prescribing constitute the cornerstone for guiding ASP's interventions. Between 2016 and 2018, the World Health Organization (WHO) collated data on antibiotic consumption for the year 2015 from 65 countries. The report found wide discrepancies in consumptions rates between countries, ranging from approximately four defined daily doses (DDD)/1000 inhabitants per day to more than 64 DDD.[6] Although antimicrobial stewardship is recommended by the Brazilian government, antimicrobial consumption data in Brazilian hospitals are scarce.[7-8]

A point prevalence survey (PPS) is one widely used approach for obtaining information about antimicrobial prescribing practices in hospitals worldwide.[9-10] It is a feasible method to access data on antimicrobial use and the results can be used for identifying targets for intervention.[11] This study aimed to evaluate the variation in antibiotic use across Brazilian hospitals that joined the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) project in 2017.

Materials and methods

Study design and setting

Brazil is the largest South American country with approximately 210,000,000 inhabitants, according to the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística - IBGE). The total area is geopolitically divided into five macro regions: Mid-West, Northeast, North, Southeast, and South, which are divided into 26 states split into over 5500 municipalities.[12] The Southeast and South are the most socioeconomically developed regions.[13]

In 2017, 60 Brazilian hospitals from three Brazilian regions (Northeast, South and Southeast) were invited to participate in the Global-PPS by email and Whatsapp workgroups. The Global-PPS is an international project, funded by bioMérieux, based on three previous PPSs carried out by the European Surveillance of Antimicrobial Consumption (ESAC).[11,14]

The study was conducted in 18 Brazilian hospitals from six states distributed among three the three target regions (Northeast, South and Southeast). The participating hospitals were located in Fortaleza, Londrina, Maringa, Recife, Rio de Janeiro, Salvador and Sao Paulo.

Ethics

This study was reviewed and approved by the Ethics and Health Research Review Committee of the coordinating centre in Brazil and each participating hospital. No identifiers were recorded to ensure anonymity. There was no contact with patients and patient consent was not required.

Data collection

The survey was conducted during one day by infection control teams. Data collection was mostly undertaken by Infectious Diseases physicians (one or two per hospital); nurses assisted in data collection in one hospital only, and there was no participation by pharmacists. All wards were audited once. All inpatients who were in the ward at 0800 h were included. Total ward inclusion at the hospital level was requested but not mandatory. Large hospitals (more than 500 beds) had the option of choosing one or more wards.

The required data were gathered by reviewing the patients' case notes and prescribing charts. The data collected included details about the numbers of inpatients in each ward (denominator). For each patient on antimicrobials (numerator), information was collected about patient characteristics; details on antimicrobial agents used (e.g. dose, dosing frequency and route of administration); and diagnosis and indication (treatment or prophylaxis). Regarding therapeutic use, we recorded whether antimicrobials were prescribed for community-acquired (CAI) or healthcare-associated infections (HAI); and for prophylaxis, whether medical (MP) or surgical (SP). Data about duration of SP were also documented. All hospitals used the National Health Surveillance Agency (ANVISA) surveillance criteria for HAI, a Brazilian guideline for infection definitions adapted from CDC/NHSN surveillance definitions and criteria for HAI.[15]

In addition, a set of quality indicators were evaluated, including reasons in notes, guideline compliance and a documented stop or review of antimicrobials in medical records.

Finally, information regarding empirical or targeted treatment (based upon microbiological result from a clinical specimen and not screening as well as any other microbiology result like for example legionella urinary antigen) and whether it was based on biomarker (e.g. CRP, procalcitonin) data was also recorded. If the antimicrobial treatment choice was based on microbiological data, we collected information on the targeted multidrug-resistant organisms (MDRO). All hospitals had microbiology laboratory support to diagnose the targeted MDRO searched by Global-PPS. All data were imputed into the Global-PPS program, a free internet-based system developed for data entry, validation and reporting to participating hospitals (www.global-pps.com).

Data analysis

Antimicrobial use was reported as the number of patients on antimicrobials (therapeutic or prophylactic use) and the number of therapies or prophylaxis. Therapy was defined as the use of one drug in one route of administration. Antimicrobial prescribing rates and the quality indicators are expressed as percentages (proportional use), means and/or ranges aggregated at regional level, by ward type, by indication (therapeutic or prophylactic use). We also ranked the number of antimicrobials for systemic use (according to the WHO ATC classification).[16]

Results

A total of 152 wards (131 adult wards and 21 paediatric wards) of 18 hospitals were included in the survey, accounting for 1801 patients (1622 adults and 179 children and neonates). Regarding the ward type, 68 were medical, 31 surgical and 53 intensive care units. The sizes of hospitals varied greatly, from one hospital with less than 50 beds to three hospitals with more than 500 beds. Most hospitals (11/18) have 100 to 499 beds. Most of the hospitals were private (11/18), tertiary (15/18) and non-teaching (11/18) institutions, providing acute and general medical and surgical services.

Out of 1801 inpatients, 941 (52.2%) were on antimicrobials on the day of the PPS. Regarding characteristics of patients on antimicrobials, 492 (52.1%) were male and most of them were adults (89,7%) (mean age, 58 years – ranging from 18 to 100 years). Antimicrobial use was higher in the Northeast region (60.4%) compared to South and Southeast regions (48.6% and 49.6%, respectively). Adult and paediatric intensive care units showed the highest prevalence of antibiotic use (60.3% and 71.1%, respectively) (table I).

The overall proportion of patients treated with more than one antimicrobial agent was 42.5% (309 patients receiving two drugs, 66 receiving three drugs, and 25 more than three drugs, respectively). Comparing the regions, there was a higher proportion of patients on at least two antimicrobials in South (48.7%) in relation to Southeast and Northeast (42% and 41.7%, respectively).

A total of 1465 antimicrobial prescriptions were evaluated. According to the ATC classification system, antibacterials for systemic use (J01) accounted for 1317 (89.9%) prescriptions, antimycotics for systemic use (J02) for 79

(5.4%), antimycobacterials (J04) for 21 (1.4%), antivirals for systemic use (J05) for 19 (1.3%), antiprotozoals (P01) for 23 (1.6%) and intestinal antiinfective agents (A07) for six (0.4%).

Among the 45 different agents amongst the 1317 antibacterials prescribed for systemic use (J01 ATC), the overall most frequent antibiotics prescribed were ceftriaxone (12.8%), meropenem (12.3%), vancomycin (10.3%) and piperacillin with a beta-lactamase inhibitor (9.3%); these four antibiotics accounted for 587 (44.6%) prescriptions. The most common indications for antibiotic therapeutic use were pneumonia or lower respiratory tract infection (29.2%), intra-abdominal sepsis (12.5%), bone or joint infections (9.5%), skin and soft tissue infection including surgical site infection (7.7%) and sepsis with no clear anatomic site (6.3%) – accounting for 698 (65.2%) prescriptions (table II). Regarding the most prescribed antibiotics and the respective indications, ceftriaxone was mainly used to treat pneumonia or LTRI (37.5%), urinary tract infection (UTI) (lower UTI - 10.1%; upper UTI -10.1%) and intra-abdominal sepsis (9.5%). Meropenem, piperacillin with a beta-lactamase inhibitor and vancomycin were mainly prescribed as therapy for pneumonia or LRTI (ranging from 17 to 41%), intra-abdominal sepsis (ranging from 14.8 to 15.6%) and sepsis with no clear anatomic site (ranging from 7.4 to 13.6%). Bone or joint infections were also frequent reasons for treatment with meropenem (9.3%) and vancomycin (11.9%).

A total of 514 (39%) antibiotics were prescribed for CAI and ceftriaxone was by far the most used (26.4%) (figure 1). Of

the 533 (40.5%) antibiotics prescribed for the treatment of HAI, meropenem (24.2%) was the first most prescribed, followed by vancomycin (18.4%) (figure 2). MP and SP accounted for 18.8% (248) of the total of antibiotics prescribed. Cefazolin was the most commonly prescribed antibiotic for SP (accounting for 111 [62.4%] of the 178 prescriptions). The prevalence of patients with at least one HAI was 19.1% (344 of 1801 inpatients) (give ratio's for different regions). Overall, 40.5% of all antibiotics for systemic use were prescribed for a HAI, with highest number of antibiotics found in the South (49.5%) (table III). Antibiotics prescribed for HAI were more frequent in intensive care units (55.5%) compared to non-critical units (30.5%), as well as in adult units (40.3%) compared to paediatric units (33.9%).

The administration route for antibiotics was parenteral (98.7% of the antibiotic prescriptions for HAI and 89.7% for CAI). Empirical use was higher for CAI (86.6%) compared to HAI (65.9%). The only biomarker used to guide treatment was C-reactive protein (CRP), used in CAI (21.8%) and HAI (33.8%). Guideline compliance of the antibiotic prescriptions for CAI was 82.7% and 83.1% for HAI (table IV). All hospitals had guidelines or protocols for antimicrobial use. Only 4.8% of the antibiotics were prescribed for infections that are not described in local guidelines.

Of 69 targeted treatments for CAI and 182 for HAI, 20 (29%) and 150 (83.5%) were against MDRO, respectively. Gram-negative bacteria accounted for 75% of the MDRO of CAI and 78.2% of HAI (table V). Although vancomycin was the third most frequent antibiotic prescribed, this drug was used mainly empirically and only about 13% of the vancomycin prescriptions (18 of 135) were guided by a multidrug-resistant Gram-positive isolate.

Discussion

We conducted for the first time a large-scale point prevalence survey on antimicrobial use at the patient level in Brazilian hospitals as part of an international study – the Global-PPS. Point prevalence surveys have been proven to be a simple and efficient method that provides useful data on antimicrobial prescribing patterns in order to determine targets for improving antibiotic use and guiding antimicrobial stewardship programmes.[11,17]

Our study showed a high prevalence of antimicrobial use (52.2%) that varied between the surveyed regions (ranging from 48.6% in the south to 60.4% in the northeast). These rates are higher than the prevalence rates reported in the previous Global-PPS in European countries (ranging from 27.4% in the eastern Europe to 39% in the Southern Europe), as well as some low- and middle-income countries (around 37% in Latin America).[10] The difference in antimicrobial use between regions is reinforced by previous analysis of the nationwide impact of a restrictive law on over-the-counter sales of antimicrobial drugs in Brazil in 2010, that showed that the drop in sales was higher in the South and Southeast, compared to the North, Northeast and Mid-West. [18] As reported in other point prevalence surveys, intensive care units reported the highest prevalence of antimicrobial use.[19-20] This study also highlights the high proportion of combination therapy (43.2%), approximately the same reported in a survey conducted in French hospitals (40.6%) and much greater than the proportion in another study with hospitals in Singapore (22.2%).[21-22]

A finding that draws attention is the high proportion of antibiotics prescribed for HAI in Brazil in 2017 (40.5%) compared to the overall proportion for the same indication reported in the survey conducted at hospitals around the world in 2015 (25.2%; ranging from 9.5% in Africa to 34.9% in Latin America).[10] At patient level, the prevalence of patients receiving antimicrobials for at least one HAI (19,1%) was considerably higher than the overall prevalence reported in the ECDC survey conducted in 30 European countries (6%).[9] It may be due the predominance of tertiary hospitals in our survey and the high proportion of patients admitted in intensive care units as well. It also suggests the overuse of antibiotics in Brazil. These data confirm the significantly higher burden of HAI in low- and middle-income countries compared to high-income countries. [23]

Overall, as reported in most countries, β-lactams were the most frequently prescribed antibiotic class in our survey. Ceftriaxone, a third-generation cephalosporin, was the most used antibiotic for CAI, followed by piperacillin with a beta-lactamase inhibitor, which may suggest that at least a proportion of these prescriptions are inappropriate. Another remarkable finding was the high proportion of use of broad-spectrum antibiotics for HAI, with meropenem representing approximately a quarter of all antibiotics prescribed, followed by vancomycin, piperacillin with a beta-lactamase inhibitor and polymixins B and E. These results could be explained in part by the high rates of antimicrobial resistance, particularly in Gram-negative organisms, reported in Brazilian ICUs.[24] However, only approximately one third of the overall treatments for HAI were targeted (guided by microbiological result). Of 135 vancomycin prescriptions, only 18 were guided by a multidrug-resistant Gram-positive isolate. This likely suggests misuse of broad-spectrum antibiotics in

Brazilian hospitals. As a limitation of a point prevalence survey, with no follow up until the completion of treatment, it was not possible to assess the rate of de-escalation therapy.

The most common diagnosis reported in our survey was pneumonia or lower respiratory tract infection, corresponding to almost 30% of all indications for antibiotic use. Although pneumonia or lower respiratory infection has been reported as the most frequent diagnosis in other surveys, the frequency does not usually exceed 20% of all diagnoses, our study showed a higher proportion.[17,25,26]

Although adherence to guidelines was surprisingly high (greater than 80%), other findings of our survey suggested inappropriate antibiotic prescribing and could be used by the participating hospitals as targets for improving antibiotic usage. Of note was the very high rates of parenteral administration, 98.7% for HAI and 89.7% for CAI. This together with the high rates of empirical therapy (86.6% in CAI and 65.9% in HAI) might be due to a lack of intravenous to oral antibiotic switch therapy protocols as well as lack of antibiotic de-escalation strategies at the participating hospitals. One important limitation of our study that would probably impact the guideline compliance was the inability of assessing the duration of therapy, once there was no follow up until the end of treatment as previously described.

This study has limitations that might affected the representativeness of the results such as the voluntary participation and the number of hospitals located in São Paulo, the major and richest city in the country. One third of the participating hospitals didn't surveyed all the wards, but only the intensive care units, which may have contributed to the higher use of broad-spectrum

antibiotics, particularly in the south region. On the other hand, it represents an important step to establish a national network of hospitals, as part of an international assessment of antimicrobial prescribing and resistance worldwide.

Conclusions

This large-scale study illustrated a high prevalence of antimicrobial use in Brazilian hospitals, higher than described in other low and middle-income countries. β-lactam antibiotics were the most frequently prescribed class of antimicrobials and the proportion of patients using two or more drugs was higher than on other countries. Although the compliance to guidelines was high, most of antimicrobials were used empirically. Participants should use these data as part of an antimicrobial stewardship program to set tailor-made targets to improve antibiotic prescribing in their hospitals.

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Conflict of interest statement

Declarations of interest: none.

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References

[1] Cosgrove SE. The Relationship between Antimicrobial Resistance and Patient Outcomes: Mortality, Length of Hospital Stay, and Health Care Costs. Clin Infect Dis 2006;42:S82–9. https://doi:10.1086/499406.

[2] Jones RN, Guzman-Blanco M, Gales AC, Gallegos B, Castro ALL, Martino MDV, et al. Susceptibility rates in Latin American nations: Report from a regional resistance surveillance program (2011). Brazilian J Infect Dis 2013;17:672–81. https://doi:10.1016/j.bjid.2013.07.002.

[3] Karlowsky JA, Hoban DJ, Hackel MA, Lob SH, Sahm DF. Resistance among Gram-negative ESKAPE pathogens isolated from hospitalized patients with intra-abdominal and urinary tract infections in Latin American countries: SMART 2013–2015. Brazilian J Infect Dis 2017;21:343–8. https://doi:10.1016/j.bjid.2017.03.006.

[4] Paterson DL. The Role of Antimicrobial Management Programs in Optimizing Antibiotic Prescribing within Hospitals. Clin Infect Dis 2006;42:S90–5. https://doi:10.1086/499407.

[5] CDC. Antibiotic Use in the United States, 2017: Progress and Opportunities. Atlanta, GA: US Department of Health and Human Services, CDC; 2017.

[6] WHO Report on Surveillance of Antibiotic Consumption. 2016-2018 early implementation. Geneva: World Health Organization; 2018. ISBN 978-92-4-151488-0. Licence: CC BY-NC-SA 3.0 IGO. https://apps.who.int/iris/bitstream/handle/10665/277359/9789241514880-

365 eng.pdf?ua=1 (accessed 17 June 2019).

366 [7] Rodrigues F d'Athayde, Bertoldi AD. The profile of antimicrobial utilization
367 in a private hospital. Cien Saude Colet. Brazil, 2010;15:1239–47.

368 [8] Wirtz VJ, Dreser A, Gonzales R. Trends in antibiotic utilization in eight
369 Latin American countries, 1997–2007. Rev Panam Salud Publica/Pan Am
370 J Public Heal 2010;27:219–25. https://doi:10.1590/S1020-
371 49892010000300009.

372 [9] European Centre for Disease Prevention and Control (ECDC). Point
373 prevalence survey of healthcare-associated infections and antimicrobial
374 use in European acute care hospitals. Stockholm: ECDC; 2013.
375 http://ecdc.europa.eu/en/publications/Publications/healthcare-associated-
376 infections-antimicrobial-use-PPS.pdf (accessed 18 February 2019).

377 [10] Versporten A, Zarb P, Caniaux I, Gros MF, Drapier N, Miller M, et al.
378 Antimicrobial consumption and resistance in adult hospital inpatients in 53
379 countries: results of an internet-based global point prevalence survey.
380 Lancet Glob Heal 2018;6:e619–29. https://doi:10.1016/S2214-
381 109X(18)30186-4.

382 [11] Zarb P, Amadeo B, Muller A, Drapier N, Vankerckhoven V, Davey P, et al.
383 Identification of targets for quality improvement in antimicrobial
384 prescribing: The web-based ESAC point prevalence survey 2009. J
385 Antimicrob Chemother 2011;66:443–9. https://doi:10.1093/jac/dkq430.

386 [12] Instituto Brasileiro de Geografia e Estatística.
387 https://www.ibge.gov.br/geociencias/organizacao-do-territorio/divisao-
388 regional.html (accessed 21 June 2019).

[13] Instituto Brasileiro de Geografia e Estatística. Atlas geográfico escolar / IBGE. – 8. ed. - Rio de Janeiro : IBGE, 2018. 224p. : il.

[14] Ansari F, Erntell M, Goossens H, Davey P. The European Surveillance of Antimicrobial Consumption (ESAC) Point-Prevalence Survey of Antibacterial Use in 20 European Hospitals in 2006. Clin Infect Dis 2009;49:1496–504. https://doi:10.1086/644617.

[15] BRASIL. ANVISA. Critérios Diagnósticos de Infecções Relacionadas à Assistência à Saúde/Agência Nacional de Vigilância Sanitária. Brasília: Anvisa, 2017. http://portal.anvisa.gov.br/documents/33852/3507912/Caderno+2+-+Critérios+Diagnósticos+de+Infecção+Relacionada+à+Assistência+à+Saúde/7485b45a-074f-4b34-8868-61f1e5724501 (accessed 21 October 2019).

[16] WHO Collaborating Centre for Drug Statistics Methodology. Anatomical Therapeutic Chemical (ATC) classification system: guidelines for ATC classification and DDD assignment 2018. http://www.whocc.no/ (accessed 18 February 2019).

[17] Willemsen I, Groenhuijzen A, Bogaers D, Stuurman A, Van Keulen P, Kluytmans J. Appropriateness of antimicrobial therapy measured by repeated prevalence surveys. Antimicrob Agents Chemother 2007;51:864–7. https://doi:10.1128/AAC.00994-06.

[18] Moura ML, Boszczowski I, Mortari N, Barrozo LV, Neto FC, Lobo RD, et al. The impact of restricting over-the-counter sales of antimicrobial drugs: Preliminary analysis of national data. Med (United States) 2015;94:1–8.

https://doi:10.1097/MD.0000000000001605.

[19] Black E, Neville H, Losier M, Harrison M, Abbass K, Slayter K, et al. Antimicrobial Use at Acute Care Hospitals in Nova Scotia: A Point Prevalence Survey. CJHP 2018;71:234–42.

[20] Giaccone P, Sinatra II, Carubia L, Marchese V, Aprea L, Mammina C, et al. Prevalence survey of healthcare-associated infections and antimicrobial use at the University. J Prev Med Hyg 2013;54:200–4.

[21] Robert J, Péan Y, Varon E, Bru JP, Bedos JP, Bertrand X, et al. Point prevalence survey of antibiotic use in French hospitals in 2009. J Antimicrob Chemother 2012;67:1020–6. https://doi:10.1093/jac/dkr571.

[22] Cai Y, Venkatachalam I, Tee NW, Yen Tan T, Kurup A, Wong SY, et al. Prevalence of healthcare-associated infections and antimicrobial use among adult inpatients in Singapore acute-care hospitals: Results from the first national point prevalence survey. Clin Infect Dis 2017;64:S61–7. https://doi:10.1093/cid/cix103.

[23] Report on the Burden of Endemic Health Care-Associated Infection Worldwide Clean Care is Safer Care. 2011. ISBN: 9789241501507. http://www.who.int (accessed 18 February 2019).

[24] BRASIL. ANVISA. Boletim de Segurança do Paciente e Qualidade em Serviços de Saúde n 17: Avaliação dos indicadores nacionais das Infecções Relacionadas à Assistência à Saúde (IRAS) e Resistência microbiana do ano de 2017. 2017. https://www20.anvisa.gov.br/segurancadopaciente/index.php/publicacoes/item/boletim-seguranca-do-paciente-e-qualidade-em-servicos-de-saude

(accessed 21 June 2019).

[25] Cotta MO, Chen C, Tacey M, James RS, Buising KL, Marshall C, et al. What are the similarities and differences in antimicrobial prescribing between Australian public and private hospitals? Intern Med J 2016;46:1182–8. https://doi:10.1111/imj.13209.

[26] Lee C, Walker SAN, Daneman N, Elligsen M, Palmay L, Coburn B, et al. Point prevalence survey of antimicrobial utilization in a Canadian tertiary-care teaching hospital. J Epidemiol Glob Health 2015;5:143–50. https://doi:10.1016/j.jegh.2014.06.003.

Tables

Table I: Antimicrobial use in adult, paediatric and neonatal inpatients, by Brazilian region and unit type, 2017.

Region	Hospitals	AMW		ASW		AICU		ASPW		Total	
	(n)	Admitted (n)	AU (%)	Admitted (n)	AU (%)	Admitted (n)	AU (%)	Admitted (n)	AU (%)	Admitted (n)	AU (%)
Northeast	6	157	54.1	63	61.9	165	67.9	25	48	410	60.5
Southeast	10	384	54.4	352	40.1	278	53.6	98	49	1112	49.2
South	2	38	47.4	37	21.6	25	84	-	-	100	47
Total	18	579	53.9	452	45.6	468	60.3	123	48.8	1622	51.9
Region	**Hospitals**	**PMW**		**PSW**		**PICU**		**NICU**		**Total**	
	(n)	Admitted (n)	AU (%)	Admitted (n)	AU (%)	Admitted (n)	AU (%)	Admitted (n)	AU (%)	Admitted (n)	AU (%)

Northeast	6	28	46.4	-	-	16	81.2	-	-	44	59.1
Southeast	10	57	63.2	9	11.1	24	62.5	34	41.2	124	53.2
South	2	-	-	-	-	5	80	6	50	11	63.6
Total	18	85	57.6	9	11.1	45	71.1	40	42	179	55.3

Diagnosis Total Northeast Southeast South

AU, antimicrobial use; AMW, adult medical wards; ASW, adult surgical wards; AICU, adult intensive-care units; ASPW, adult specialized wards; PMW, paediatric medical wards; PSW, paediatric surgical wards; PICU, paediatric intensive-care units; NICU, neonatal intensive-care units.

Table II: Most common diagnosis for antibiotic therapeutic use in 18 hospitals by Brazilian region, 2017.

	n (%)	n (%)	n (%)	n (%)
Pneumonia or lower respiratory tract infection	312 (29.2)	109 (35.3)	155 (23.7)	48 (45.3)
Intra-abdominal sepsis	134 (12.5)	33 (10.7)	86 (13.2)	15 (14.2)
Bone or joint infection	102 (9.5)	15 (4.9)	85 (13.0)	2 (1.9)
Skin and soft tissue infection	82 (7.7)	21 (6.8)	56 (8.6)	5 (4.7)
Sepsis	67 (6.3)	20 (6.5)	46 (7.0)	1 (0.9)
Upper urinary tract infection	53 (5.0)	28 (9.1)	21 (3.2)	4 (3.8)
Lower urinary tract infection	51 (4.8)	11 (3.6)	33 (5.1)	7 (6.6)
Gastrointestinal infection	35 (3.3)	9 (2.9)	26 (4.0)	0
Bacteraemia with no clear anatomical site	31 (2.9)	9 (2.9)	17 (2.6)	5 (4.7)
Fever in the neutropaenic patient	30 (2.8)	11 (3.6)	12 (1.8)	7 (6.6)
Therapy for ear, nose, throat infections including mouth, sinuses, larynx	30 (2.8)	3 (0.9)	22 (3.4)	5 (4.7)
All other diagnosis	142 (13.3)	40 (12.9)	95 (14.5)	7 (6.6)
Total	1069	309	654	106

Table III: Antibiotic use by indication and Brazilian region, 2017.

Region	Total antibiotic prescriptions	CAI	HAI	Surgical prophylaxis	Medical prophylaxis	Other indication	Unknown indication
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Northeast	377	161 (42.7)	140 (37.1)	45 (11.9)	23 (6.1)	3 (0.8)	5 (1.3)
Southeast	829	302 (36.4)	339 (40.9)	129 (15.6)	46 (5.6)	2 (0.2)	12 (1.4)
South	111	51 (45.9)	55 (49.5)	4 (3.6)	1 (0.9)	0	0
Total	1317	514 (39)	533 (40.5)	178 (13.5)	70 (5.3)	5 (0.4)	17 (1.3)

CAI, community-acquired infections; HAI, healthcare-associated infections.

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534 Table IV: Antibiotic prescription patterns and antibiotic quality indicators by Brazilian region, 2017.
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	Antibiotic prescriptions	Reason in notes n (%)	Stop or review date recorded n (%)	Parenteral administration n (%)	Guideline compliance n (%)	Biomarker use (CRP) n (%)	Targeted treatment n (%)	Targeted treatment (resistant organism) n (%)
Community-acquired infections								
Northeast	161	146 (90.7)	58 (36)	150 (93.2)	135 (83.8)	17 (10.6)	26 (16.2)	4 (2.5)
Southeast	302	283 (93.7)	186 (61.6)	262 (86.8)	251 (83.1)	85 (28.1)	38 (12.6)	14 (4.6)
South	51	50 (98)	48 (94.1)	49 (96.1)	39 (76.5)	10 (19.6)	5 (9.8)	2 (3.9)
Total	514	479 (93.2)	292 (56.8)	461 (89.7)	425 (82.7)	112 (21.8)	69 (13.4)	20 (3.9)
Healthcare-associated infections								
	Antibiotic prescriptions	**Reason in notes**	**Stop or review date recorded**	**Parenteral administration**	**Guideline compliance**	**Biomarker use (CRP)**	**Targeted treatment**	**Targeted treatment (resistant**

		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	**organism)** n (%)
Northeast	140	137 (97.9)	87 (62.1)	135 (96.4)	119 (85)	48 (34.3)	65 (46.4)	52 (37.1)
Southeast	338	310 (91.7)	243 (71.9)	336 (99.4)	276 (81.7)	91 (26.9)	99 (29.3)	83 (24.6)
South	55	54 (98.2)	48 (87.3)	55 (100)	48 (87.3)	41 (74.5)	18 (32.7)	17 (30.9)
Total	533	501 (94)	378 (70.9)	526 (98.7)	443 (83.1)	180 (33.8)	182 (35.1)	152 (28.5)

CRP, c-reactive protein

Table V: Prevalence of antimicrobial resistant organisms in inpatients who received targeted antibiotics by Brazilian region, 2017.

Community-acquired infections									
	MRSA	**MRCoNS**	**VRE**	**ESBL**	**3GCREB**	**CRE**	**CR-NFGNB**	**Other MDRO**	**Total**
Northeast	-	-	-	3 (75)	1 (25)	-	-	-	4
Southeast	1 (7,1)	1 (7,1)	-	2 (14,3)	1 (7,1)	2 (14,3)	5 (35,7)	2 (14,3)	14
South	-	-	-	1 (50)	-	-	-	1 (50)	2
Total	1 (5)	1 (5)	-	6 (30)	2 (10)	2 (10)	5 (25)	3 (15)	20
Healthcare-associated infections									
	MRSA	**MRCoNS**	**VRE**	**ESBL**	**3GCREB**	**CRE**	**CR-NFGNB**	**Other MDRO**	**Total**
Northeast	-	1 (1,9)	1 (1,9)	8 (15,4)	3 (5,8)	12 (23,1)	23 (44,2)	4 (7,7)	52
Southeast	10 (12,1)	8 (9,6)	8 (9,6)	12 (14,5)	6 (7,2)	17 (20,5)	17 (20,5)	5 (6)	83
South	2 (11,8)	2 (11,8)	-	3 (17,6)	1 (5,9)	3 (17,6)	5 (29,4)	1 (5,9)	17

Total	12 (7,9)	11 (7,2)	9 (5,9)	23 (15,1)	10 (6,6)	32 (21,1)	45 (29,6)	10 (6,6)	152

MRSA, meticillin-resistant *Staphylococcus aureus*; MRCoNS, meticillin-resistant coagulase-negative staphylococci; VRE, vancomycin-resistant enterococci; ESBL, Extended-spectrum β-lactamases; 3GCREB, third-generation cephalosporin-resistant Enterobacteriaceae (Non-ESBL producing or ESBL status unknown); CRE, Carbapenem-resistant Enterobacteriaceae; CR-NFGNB, Carbapenem-resistant non-fermenting Gram-negative bacilli; MDRO, multidrug-resistant organism.

Figures

Figure 1: Proportion of the most frequent antibiotics for systemic use prescribed for community-acquired infection by Brazilian region, 2017.

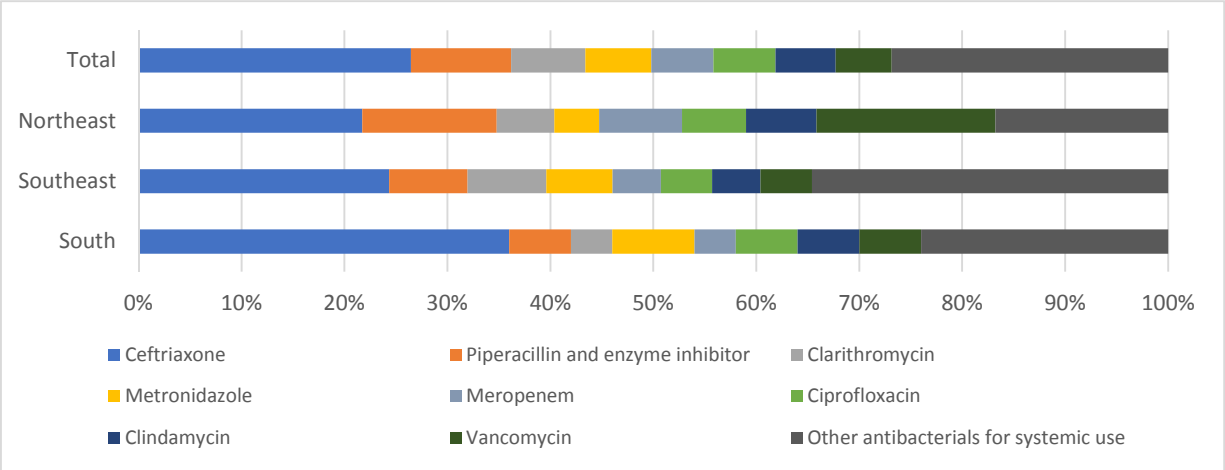
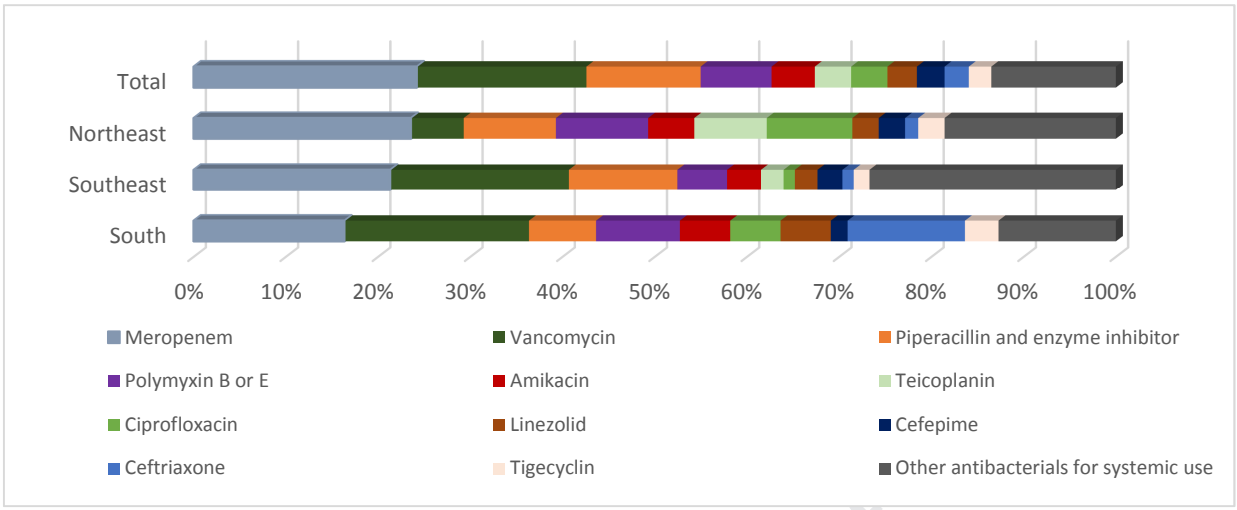


Figure 2: Proportion of the most frequent antibiotics for systemic use prescribed for healthcare-associated infection by Brazilian region, 2017.



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632 **Legends**

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634 AU = antimicrobial use;

635 AMW = adult medical wards

636 ASW = adult surgical wards

637 AICU = adult intensive-care units

638 ASPW = adult specialized wards.

639 PMW = paediatric medical wards

640 PSW = paediatric surgical wards

641 PICU = paediatric intensive-care units

642 NICU = neonatal intensive-care units

643 CAI = community-acquired infections

644 HAI = healthcare-associated infections

645 CRP = C-reactive protein

646 MRSA = meticillin-resistant *Staphylococcus aureus*

647 MRCoNS = meticillin-resistant coagulase-negative staphylococci

648 VRE = vancomycin-resistant enterococci

649 ESBL = Extended-spectrum β-lactamases

650 3GCREB, third-generation cephalosporin-resistant Enterobacteriaceae (Non-

651 ESBL producing or ESBL status unknown)

652 CRE = Carbapenem-resistant Enterobacteriaceae

653 CR-NFGNB = Carbapenem-resistant non-fermenting Gram-negative bacilli

654 MDRO = multidrug-resistant organism.