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Establishing nationally representative central line-associated bloodstream infection surveillance data for paediatric patients in Greece

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SUMMARY

Background: Healthcare-associated infections (HCAIs) are associated with increased morbidity and mortality and with excess costs. Central line-associated bloodstream infections (CLABSIs) are the most common HCAIs in neonates and children.
Aim: To establish national benchmark data for rates of CLABSI in neonatal and paediatric intensive care units (NICUs and PICUs) and paediatric oncology units (ONCs).
Methods: Active surveillance for CLABSI was conducted from June 2016 to February 2017. A collaborative of 14 NICUs, four PICUs, and six ONCs participated in the programme. Surveillance definitions of central line (CL), central line utilization (CLU) ratio, CLABSI event, and CLABSI rate were based on the Centers for Disease Control and Prevention's 2014 National Healthcare Safety Network criteria. Medical records were assessed daily for calculating CL-days, patient-days, and susceptibility of isolated organisms.
Findings: A total of 111 CLABSI episodes were recorded. The overall mean CLABSI rate was 4.41 infections per 1000 CL-days, and the CLU ratio was 0.31. CLABSI rates were 6.02 in NICUs, 6.09 in PICUs, and 2.78 per 1000 CL-days in ONCs. A total of 123 pathogens were isolated. The most common pathogens were Enterobacteriaceae (36%), followed by Gram-positive cocci (29%), non-fermenting Gram-negative bacteria (16%), and fungi (16%). Overall, 37% of Gram-negative pathogens were resistant to third-generation cephalosporins and 37% to carbapenems.

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[1] See Appendix A.

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Conclusion: Nationally representative CLABSI rates were determined for paediatric patients. These data could be used to benchmark and serve as baseline data for the design and evaluation of infection control and antimicrobial stewardship interventions.

Introduction

Healthcare-associated infections (HCAIs) are linked with increased morbidity and mortality and with excess costs. A significant proportion of HCAIs are preventable. Thus, they are considered to be an important metric of patient safety and quality of care [1].

HCAIs often occur due to the presence of antibiotic-resistant pathogens, which are increasingly prevalent and are also associated with significant morbidity, mortality, and excess costs. The problem of antimicrobial resistance (AMR), considered a growing threat to global public health, overlaps significantly with HCAIs. HCAIs trigger the use of broad-spectrum antibiotics, further driving the emergence of multidrug-resistant organisms [2,3]. During the last decade, the reduction of HCAI and maintaining zero incidences has become a major focus of attention in healthcare systems worldwide. Many healthcare systems set the goal of sustaining zero CLABSI events in the long term [4].

In Greece, data suggest that up to 10% of hospitalized patients develop an HCAI, many of which are due to AMR organisms. Rates of AMR in Greek hospitals are among the highest in Europe [5].

Paediatric patients who require intensive care are at increased risk for HCAI. Central venous catheters (CVCs) are often used for therapeutic interventions in these patients, yet their use is not without risk. One of the most common complications associated with CVC use is central line-associated bloodstream infection (CLABSI). CLABSIs are the most common HCAIs in neonates and children [6—8]. However, it has been shown that CLABSIs are preventable, and their prevention requires an approach based on systematic surveillance and intervention [9—12]. In Greece the most recent surveillance data come from individual studies and point-prevalence surveys [13—17].

This study aimed to establish national benchmark data for rates of CLABSI in Greek neonatal intensive care units (NICUs), paediatric intensive care units (PICUs) and paediatric oncology units (ONCs), to support the long-term goal of reducing CLABSI rates and improving the quality of patient care.

Methods

Study design

The study was conducted by active surveillance for CLABSIs over a nine-month period between June 2016 and February 2017.

Study setting

A national collaborative, called Preventing Hospital-acquired Infections in Greece (PHIG), was developed with the ultimate goal of reducing CLABSI rates nationally. The NICUs ($N = 14$), PICUs ($N = 4$), and ONCs ($N = 6$) from all state hospitals across the country participated in this initiative, with the exception of one that was enlisted at the beginning but withdrawn some months later.

Each unit had assigned an on-site investigator that was in charge of data collection and used positive blood cultures as a trigger for CLABSI investigation. All local investigators were trained in the methodology by a group of four experienced infection prevention specialists that also oversaw and aided data collection in order to achieve consistent application of methodology. Units were categorized by medical school affiliation and unit bed size. A 'major teaching hospital' was defined as a hospital with a programme for medical and postgraduate students. A 'graduate hospital' was defined as a hospital with only residency and/or fellowship training programmes.

Data sources and definitions

Data collection tools were designed for the purpose of surveillance of CLABSI. Surveillance was conducted prospectively, and data were collected from medical records by an on-site investigator who was in charge of data collection and who used positive blood cultures as a trigger for CLABSI investigation. All local investigators were trained in the methodology by a group of four experienced infection prevention specialists who also oversaw and aided data collection in order to achieve consistent application of methodology. Microbiological data, including the susceptibilities of the isolated organisms, were also recorded.

The definitions of central line (CL), central line utilization ratio (CLU ratio), CLABSI event, and CLABSI rate were based on the Centers for Disease Control and Prevention (CDC) 2014 National Healthcare Safety Network (NHSN) criteria [18].

CLABSI was defined as a laboratory-confirmed bloodstream infection based on a single blood culture for organisms not commonly present on the skin, and two or more blood cultures for organisms commonly present on the skin, in a patient who was hospitalized for at least two days and who had a CL at the time of infection or within two calendar days before. In addition, the infection could not be secondary to an infection at another body site.

For patients having a previous CLABSI diagnosis, reinfection was considered if there was a negative blood culture and an absence of symptoms between episodes [18].

Denominator data, CL-days, and patient-days were collected manually on a daily basis, at the same time of day in every unit. The CLABSI rate was defined as the number of CLABSI events divided by the total number of CL-days, and expressed as the number of CLABSIs per 1000 CL-days. CLU ratio was defined as the number of CL-days divided by the total number of patient-days. In the NICU, CLABSI rates were stratified in each of five birth-weight categories ($\leq$750 g, 751—1000 g, 1001—1500 g, 1501—2500 g, and $>$2500 g).

Mucosal barrier injury laboratory-confirmed bloodstream infections (MBI-LCBSIs) for paediatric patients were also recorded using the CDC definition [18].

Pathogens of CLABSIs were categorized as Gram-positive cocci, Enterobacteriaceae, non-fermenting Gram-negative pathogens, and fungi. MDR organisms were defined as those exhibiting non-susceptibility to at least one agent in three or more antimicrobial categories [19].

Statistical analysis

CLABSI rates and CLU ratios are presented with median and interquartile range (25^{th} and 75^{th} percentiles) across units. Pooled means for each type of acute care facility were also calculated. A run chart was used to track changes in monthly CLABSI rates. Categorical variables (such as type of medical school affiliation and bed size of a unit) and the distribution of pathogens are presented as absolute (*N*) and relative (%) frequencies. All analyses were conducted using Stata v.13.0 statistical software.

Results

The study enrolled 24 facilities across Greece, with 30% of them categorized as 'major teaching hospitals' and the majority (80%) having a total number of beds per unit ≤30 (Table I).

A total of 111 CLABSI episodes among paediatric patients were recorded during the nine-month surveillance period. Among paediatric oncology patients, a total of 35 CLABSIs were identified during the study period, and 15 out of 35 (42.86%) were classified as MBI-LCBI (Table I). The overall mean CLABSI rate was 4.41 infections per 1000 CL-days, and the CLU was 0.31 across all participating units. The monthly CLABSI rates for all units across the whole surveillance period are presented in Figure 1.

Stratified analysis by ward type revealed that the higher CLABSI rates were noticed in the PICUs and NICUs, and the higher CLU ratio was in ONCs (Table II). The stratification of CLABSI rates among the units were 6.02 infections per 1000 CL-days for NICUs, 6.12 for PICUs, and 2.78 for ONCs (Table II). Higher CLU ratios were reported among ONCs (0.84) and a lower ratio was found among NICUs (0.15).

In NICUs, CLABSI rates were stratified by birth-weight category: ≤750 g, 751–1000 g, 1001–1500 g, 1501–2500 g, and >2500 g and were respectively 15.29, 11.14, 6.40, 2.52, and 2.91 infections per 1000 CL-days (Table III) with higher CLABSI rates reported among the very low birth-weight infants. Similar median CLABSI rates were recorded in NICUs in major and graduate hospitals (6.8 vs 7.1 per 1000 CL-days, respectively). The most common type of CL used in NICUs was umbilical (54%) followed by peripherally inserted central catheters (PICC; 24%) and Hickman (13%).

A total of 123 pathogens isolated in 111 CLABSI episodes were observed among all units. The most common pathogens were Enterobacteriaceae (36%), followed by Gram-positive cocci (29%), non-fermenting Gram-negative bacteria (16%), and fungi (16%). The most frequently isolated pathogens were coagulase-negative staphylococci (16.3%; 20/123), *Klebsiella* spp. (16.3%; 20/123), *Candida* spp. (15.5%; 19/123), *Pseudomonas aeruginosa* (10.6%; 13/123), and *Enterobacter* spp. (8.9%; 11/123) (Table IV). Gram-positive cocci were most frequently reported in PICUs, and Enterobacteriaceae were the most common CLABSI pathogens in NICUs and ONCs.

Thirty-one out of 44 (71%) Enterobacteriaceae were categorized as MDR, 15 of which (34%) were carbapenem-resistant Enterobacteriaceae (CRE) and 22 (50%) of which were resistant to third-generation cephalosporins. Overall, 37% (25/67) of Gram-negative pathogens were resistant to carbapenems, and 37% (25/67) were resistant to third-generation cephalosporins. Half (2/4) of the *S. aureus* isolates were resistant to oxacillin, and one-quarter (2/8) of the *Enterococcus* isolates were resistant to vancomycin (VRE) (Tables IV and V).

Discussion

This study has established nationally representative CLABSI rates for paediatric patients in Greece. Comparing the CLABSI rates in PICUs and NICUs with the rates in the NHSN annual report and with data from the International Nosocomial Infection Control Consortium (INNIC) (Table II), the CLABSI rates among Greek PICUs were almost eight times higher than those in the 2013 NHSN report, but lower than INNIC, and similar CLABSI rates were recorded in NICUs in major and graduate hospitals, which is similar to the findings of Rosenthal *et al.* that CLABSI rates in NICU patients were not different in public versus academic hospitals [20,21].

Results from the Greek paediatric oncology units were similar to rates in the NHSN report [20]. The NHSN CLABSI rates per 1000 CL-days for the paediatric general haematology/oncology ward and paediatric haematopoietic stem-cell transplant ward were 2.1 and 2.4 with use of permanent CL, and 2.1 and 2.2 with use of temporary CL. In the Greek paediatric oncology units, the CLABSI rate for both permanent and temporary CLs was 2.78 infections per 1000 CL-days.

Among paediatric haematology patients, MBI-LCBI rates represented 43% of total CLABSI rates. This finding is in concurrence with the results of another large study that evaluated 1100 episodes of CLABSI in 34 paediatric haematologic

Table I
Enrolled facilities contributing data used in this report, during the surveillance period June 2016 to February 2017

Type of acute care facility	No. of locations	Unit bed size, median (IQR)	No. of CLABSIs	No. of MBI-CLABSIs	Total CL-days	Total patient-days	Total antibiotic-days	No. of days		
								25%	Median	75%
NICUs	14	26 (20–30)	55	0	9141	62,368	23,027	291	359	401
PICUs	4	7 (6–9.5)	21	0	3430	5059	2977	333	563	848
ONCs	6	18 (15.5–20.5)	35	15	12,572	14,881	8725	445	477	619
All units	24	20 (14.5–28)	111	15	25,143	82,308	34,729			

IQR, interquartile range; CLABSI, central line-related bloodstream infection; MBI, mucosal barrier injury; CL, central line; NICU, neonatal intensive care unit; PICU, paediatric intensive care unit; ONC, paediatric oncology unit.

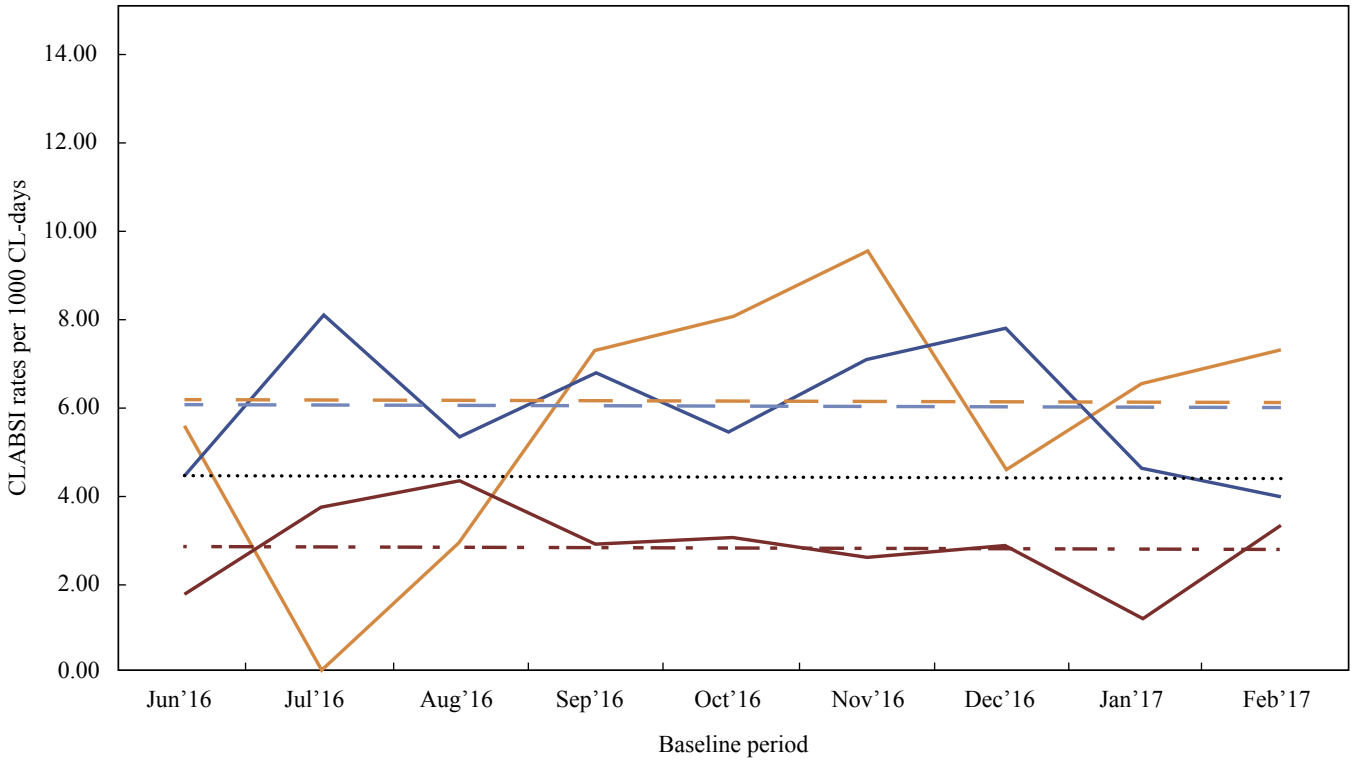

Figure 1. Monthly central line catheter bloodstream infection (CLABSI) rate and overall CLABSI rate among all units. CL, central line; NICU, neonatal intensive care unit; ONC, paediatric oncology unit; PICU, paediatric intensive care unit.

Table II
Pooled means and key percentiles of the distribution of CLABSI rates and CLU ratios by type of location: comparison with pooled means of NHSN and INNIC reports

Type of acute care facility	CLABSI rate						CLU ratio					
	Pooled mean	25%	Median	75%	NHSN report (2013)	INNIC report (2010–2015)	Pooled mean	25%	Median	75%	NHSN report (2013)	INNIC report (2010–2015)
NICUs	6.02	3.83	6.96	9.9		16.37	0.15	0.06	0.13	0.26		0.35
PICUs	6.12	4.77	6.24	16.5	0.8	8.46	0.68	0.38	0.72	0.89	0.37	0.59
ONCs	2.78	1.65	2.48	3.65	2.1	_	0.84	0.79	0.83	0.97	0.58	_

CLABSI, central line-related bloodstream infection; CLU, central line utilization; NHSN, National Health Safety Network; INNIC, International Nosocomial Infection Control Consortium; NICU, neonatal intensive care unit; PICU, paediatric intensive care unit; ONC, paediatric oncology unit.

Table III
Pooled means and key percentiles of the distribution of CLABSI rates and CLU ratios for NICUs: comparison with pooled means of NHSN and INNIC reports

NICU birth weight (g)	CLABSI rate						CLU ratio					
	Pooled mean	25%	Median	75%	NHSN report (2013)	INNIC report (2010–2015)	Pooled mean	25%	Median	75%	NHSN report (2013)	INNIC report (2010–2015)
<750	15.29	2.84	12.8	44.64	2.2	20.9	0.35	0.28	0.33	0.5	0.39	0.49
750–1000	11.14	0	13.89	27.02	1.9	8.74	0.23	0.11	0.21	0.31	0.32	0.29
1000–1500	6.40	0	0.97	8.26	1.0	19.70	0.22	0.1	0.21	0.28	0.25	0.48
1500–2500	2.52	0	0	0	0.6	20.86	0.10	0.02	0.08	0.17	0.14	0.41
≥2500	2.91	0	0	4.39	0.5	10.53	0.10	0.05	0.1	0.18	0.17	0.24
Overall	6.02	3.83	6.96	9.9		16.37	0.15	0.06	0.13	0.26		0.35

CLABSI, central line-related bloodstream infection; CLU, central line utilization; NICU, neonatal intensive care unit; NHSN, National Health Safety Network; INNIC, International Nosocomial Infection Control Consortium; PICU, paediatric intensive care unit.

Table IV
Distribution of isolated CLABSI pathogens in PICUs, NICUs and ONCs

	Total ($N = 123$)	Multidrug resistant
Gram-positive cocci	36 (29%)	4/36 (11%)
Staphylococcus aureus	4	2
Coagulase-negative staphylococci	20	
Enterococcus spp.	8	2
Streptococcus spp.	2	
Other Gram-positive	2	
Enterobacteriaceae	44 (36%)	31/44 (71%)
Enterobacter spp.	11	8
Escherichia coli	7	4
Klebsiella spp.	20	17
Serratia spp.	6	2
Non-fermenting Gram-negative pathogens	20 (16%)	9/20 (45%)
Acinetobacter spp.	3	3
Pseudomonas aeruginosa	13	6
Stenotrophomonas maltophilia	4	
Other Gram-negative	3 (2%)	
Fungi	20 (16%)	
Candida spp.	19	
Other fungi	1	

CLABSI, central line-related bloodstream infection; PICU, paediatric intensive care unit; NICU, neonatal intensive care unit; ONC, paediatric oncology unit.

centres between 2013 and 2015 and found that 51% of CLABSIs were classified as MBI [22]. This underscores the importance of preventing MBI-LCBI in this vulnerable group of patients. In neutropenic oncology patients, MBI-LCBI frequently involves translocation of oral and gastrointestinal flora into the bloodstream, and may be prevented using oral care bundles [23].

Higher CLABSI rates in our paediatric population were noted compared to ECDC data on adult ICUs from 15 European countries. According to the European Centre for Disease Prevention and Control (ECDC) annual report for 2015, the mean CLABSI rate was 3.6 infections per 1000 CL-days and CLU ratio was on average 0.7 [24]. High CLABSI rates among paediatric units in Greece may reflect a lack of appropriate policies or the weakness of implementation guidelines related to infection control practices in Greek hospitals. Low nurse:patient staffing ratio, hospital overcrowding, lack of medical supplies, and insufficient numbers of infection-control healthcare workers may also be significant factors contributing to the problem of HCAIs in Greek units [15,25,26]. On the other hand, our study shows lower CLABSI rates compared with a surveillance study conducted by the International Nosocomial Infection Control Consortium (INICC) from January 2010 through December 2015 in 703 ICUs of 50 countries in Latin America, Europe, Eastern Mediterranean, Southeast Asia and Western Pacific World Health Organization regions [27].

Among all units in the study, most of the bacterial pathogens isolated in CLABSI episodes were Enterobacteriaceae, presenting a high rate of MDR and CRE organisms, while other types of resistance that were present in our population included meticillin-resistant *Staphylococcus aureus* (MRSA) and VRE. These results are in keeping with earlier studies that have shown carbapenem resistance among Enterobacteriaceae to be a major public health issue in Greece; they confirm that many HCAIs in Greek hospitals are due to resistant organisms; and they highlight serious concerns regarding ineffective therapies and mortality rates [5,28].

Epidemiology of pathogens associated with CLABSIs varies in the literature, with some reports showing predominance of Gram-positive organisms, whereas others show a predominance of Gram-negative pathogens [29–31]. In our study, Gram-negative pathogens predominated, and these were often AMR.

Differences in the aetiology of CLABSI episodes and in the AMR profile reported in recent ECDC and NHSN reports show the need for detailed paediatric surveillance data at a European but also at a national level.

Our study has some limitations. The CLABSI rates reported herein may be subject to the possibility of surveillance bias. A low rate may be the result of inadequate infection detection or very low CLU ratio. Similarly, a high CLABSI rate does not necessarily define a problem, but it may suggest an area of further investigation.

Table V
Antibiotic resistance among Gram-negative isolate CLABSI pathogens of central line-related bloodstream infection

	N	No. (%) of resistant pathogens		
		Carbapenems	Cefotaxime/ ceftriaxone	Ceftazidime
Enterobacteriaceae	44			
Enterobacter spp.	11	4 (36%)	6 (55%)	
Escherichia coli	7	0	1 (14%)	
Klebsiella spp.	20	9 (45%)	13 (65%)	
Serratia spp.	6	2 (33%)	2 (33%)	
Non-fermenting Gram-negative pathogens	20			
Acinetobacter spp.	3	3 (100%)	2	
Pseudomonas aeruginosa	13	5 (38%)		5 (38%)
Stenotrophomonas maltophilia	4	1 (25%)	1	
Other Gram-negative	3	1 (33%)		

CLABSI, central line-related bloodstream infection.

In conclusion, this study determined CLABSI rates for high-risk children. Our rates of CLABSI and antibiotic resistance among organisms causing CLABSI were high. These data highlight the significance of this problem and emphasize the need for implementation of infection prevention interventions.

Our study also presents benchmark CLABSI rates in a large network of paediatric units in Greece that could be used for future estimations and to guide future HCAI-related interventions.

Methodology used for this surveillance programme could also be applied in other paediatric or adult units across the country. Facilities could use these data to guide local prevention efforts and to create an even wider national network for the prevention of paediatric CLABSI.

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Conflict of interest statement
None declared.

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Appendix A. PHIG (Preventing Hospital-acquired Infections in Greece) Investigators

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