ORIGINAL ARTICLE

Hospital-acquired infections and leading pathogens detected in a regional university adult acute-care hospital in Genoa, Liguria, Italy: results from a prevalence study

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Key words

Hospital-acquired infections • Prevalence • Leading pathogens

Summary

Background. *A prevalence study aimed to update the epidemiological scenario of Hospital-Acquired Infections (HAI) was performed at the San Martino University Hospital of Genoa, the Regional Reference Adult-care Center in Liguria, Italy, with more than 1300 beds.*
Materials and methods. *The investigation was performed in all the wards, except the Psychiatric Units, between 19th March and 6th April, 2007, using a one-day monitoring system for each ward. International standardized criteria and definitions for the surveillance of HAI were used for the collection of data, which were recorded in specific software for subsequent consolidation, analysis and quality control.*
Results. *The hospital infection control staff actively monitored 912 inpatients: a total of 84 HAI among 72 patients were diagnosed, with an overall prevalence of infections and affected cases of 9.2% (95% CI: 7.3-11.1) and 7.9% (95% CI: 6.1-9.7), respectively. Urinary Tract Infections (UTI) (30.9%), Respiratory Tract Infections (RTI) (28.6%) and Blood Stream Infections (BSI) (21.4%) were found to be the most frequent infections. As expected, both specific prevalence and localization of HAI varied considerably between wards, with the highest values recorded in Intensive Care Units (ICU) and in Functional Rehabilitation wards. RTI (26.3%) and BSI (13.2%) were found primarily represented in ICU, while the highest values of UTI (13.3%) were registered in Functional Rehabilitation Units. Enterococcus spp. (16.8%), Candida spp. (14%), Pseudomonas spp. (12.2), Staphylococcus aureus (10.7%), Escherichia coli (10.3%) and Coagulase-negative staphylococci (CNS) (9.3%) were the most frequent pathogens isolated. The overall rate of administration of antibiotics was 55.3% and penicillin (26.7%), cephalosporins (22.8%) and fluoroquinolones (17.9%) were found to be the leading antibacterial administered.*
Conclusion. *Results of the present study have been, and are currently, used for orientating surveillance and control hospital policies, planning activities according to a rational and evidence-based approach.*

Background

The surveillance and control of Hospital-Acquired Infections (HAI) is a public health priority in Western Countries, primarily on account of the associated health-care burden, in terms both of morbidity and mortality among affected patients [1], but also considering the indirect effects associated with onset of infection, both economic and social, such as, prolonged length of hospital stay (LOS), re-admissions or additional care, use of expensive therapies with potential occurrence of antibiotic resistance and also loss of work and social activities [2, 3].
Acute-health care settings and large teaching hospitals are the elective areas where the majority of invasive and innovative medical procedures are routinely performed, and where critically ill patients are often hospitalized: thus, there is clearly a need to strictly adhere to the existing recommended policies in the prevention of HAI, particularly in these well-known high-risk institutions [4]. In this respect, active surveillance represents the cornerstone, universally accepted for achieving optimal control [5, 6]. Adhering to this aspect of the institutional and routine patient care-process is often very difficult, particularly when the human and financial resources available are limited. This represents another reason for planning prevention policies, using an evidence-based approach (i.e., starting with correct assessment of the frequency of infections, their impact on patient health, identification of the main associated risk factors and conditions), thus ultimately orientating appropriate and corrective interventions [7-9].
During the last two years, substantial efforts have been made by the Infection Control Committee of the Liguria Region, to improve surveillance and control activities: particularly, a regional prevalence survey, monitoring

3176 hospitalized patients, was performed, in 2007, within the existing public adult and pediatric acute-care hospitals, with a reported prevalence of 8.9% cases affected by HAI [10]. Herewith, an in-depth analysis of the main results, both clinical and microbiological, emerging from the reference adult acute-care teaching hospital of Liguria, collected as part of the above-mentioned regional study, are fully reported and discussed.

Materials and methods

The investigation was performed at the San Martino University Hospital of Genoa, Italy, between 19th March and 6th April, 2007, monitoring all the hospital wards, except the Psychiatric Units. The survey, on more than 1300 beds, using a one-day monitoring system for each ward, was coordinated by the Medical Directorate of the Hospital, in close collaboration with Hygiene Unit and Infectious Diseases Unit of the University of Genoa, which were also responsible for the methods used and final validation and analysis of data. The study was possible thanks to an *ad hoc* and extraordinary setting up of a working group comprising 10 survey teams, each of which with one medical doctor and one infection control nurse. All the health-care personnel was well trained before starting the investigation, in order not only to use international standardized criteria and definitions for the surveillance of HAI [11-14], but also to record the information collected in the specific software for later consolidation, analysis and quality control. In particular, HAI was defined as an adverse reaction to the presence of an infectious agent(s) or its toxin(s) with no evidence that the infection was present, or incubating at the time of admission to the acute-care setting [14].

Empirical use of antibiotics was defined as the administration of treatment to a patient with signs and symptoms of infection, without an identified source or microbiologic isolate. Targeted therapy was defined as the administration of the antibiotic for an identified isolate.

Only patients with full-hospitalization were enrolled in the surveillance, while those transferred or discharged on the day of the analysis were excluded. All anagraphic, anamnestic and clinical data, potentially related to the onset of infection, were collected by the investigators; medical and nurses' charts as well as consultations with the specialists directly in the wards were also used as a source of data. Collection of clinical data, directly by the patients, was also performed when feasible. Results of culture-tests were also collected from all the clinically diagnosed cases, both at the time of the survey in the ward and within one month thereafter, these findings being then used in the final ascertainment of the diagnosis of the infection.

As far as concerns data analysis, prevalence was calculated for HAI (number of infections divided by the total number of patients in the study population) and for cases (number of patients with HAI divided by the total number of the study population): crude and specific rates were recorded both overall and according not only to the localization of the infection but also the ward. Relative frequencies of infection according to type were also calculated.

Descriptive analysis of the study population, including demographics and distribution of all clinical information concerning infections, together with the calculation of means, medians and confidence intervals, were performed using the Statistical Analysis System (SAS) package.

Results

Overall 912 patients were enrolled in the investigation, thus a mean hospital bed-occupation rate of 68.5%. Mean age of the population under survey was 64.6 years (SD 23.1; range: 0-107), with a female-male ratio of ~1:1. The mean pre-survey LOS accounted for 16.9 days (SD: 27.7; range: 1-400; median: 10.0): in particular the mean LOS for patients undergoing surgery (n= 312) was 6.6 days (SD: 16.0; range: 1-244; median: 2). Overall, 720 of the 912 inpatients enrolled (78.9%) had at least one condition of morbidity at the time of the study, and 593 patients (65.0%) were exposed to at least one invasive medical device, used for diagnosis or treatment. The leading specific medical conditions, and the most frequent devices used in the study population are summarized in Table I.

As far as concerns infections, a total of 84 HAI occurred in 72 patients, with relative overall prevalence of 9.2% and 7.9%: most of the patients presented a single localization (90.3%), with only 4 (5.5%) and 3 (4.2%) individuals respectively presenting 2 or 3 co-infections. The most prevalent HAI resulted Urinary Tract Infections (UTI), Respiratory Tract Infections (RTI) and

Tab. I. Leading medical conditions and most frequent devices used among the study population (n = 912).

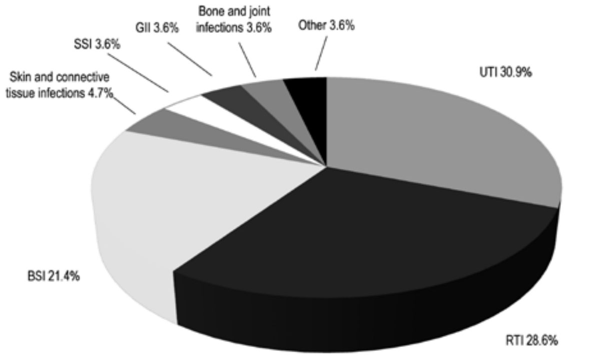
Leading medical conditions (n = 1335)	**Percentage (%)**
Cardiovascular diseases	30.3
Cancer	15.5
Diabetes	10.1
Pulmonary chronic diseases	8.5
Immunosoppresive therapy	6.7
Kidney chronic diseases	5.8
Previous infection	5.5
Other	17.6
Most frequent devices (n= 1112)	**Percentage (%)**
Peripheral venous catheter	37.1
Urinary catheter	26.1
Central venous catheter	15.5
Surgical drain	7.7
Naso-gastric tube	4.7
Endotracheal tube	2.8
Tracheal cannula	2.7
Other	3.4

Blood Stream Infections (BSI) with values of 2.9 (95% CI = 1.8-4.0), 2.6 (95% CI = 1.6-3.6) and 2.0 (95% CI=1.1-2.9), respectively. The relative frequencies of the leading infection sites are shown in Figure 1. Briefly, UTI and RTI, accounting for 30.9% and 28.6%, respectively, together with BSI (21.4%) were found to be, by far, the most predominant localizations in the hospital. With regards to BSI, 39% (7/18) of these were catheter-related bacteremia.

HAI numbers and prevalence, referred to ward, overall and according to localization, are outlined in Table II. Prevalence of HAI varied considerably between hospital units, with values ranging from 0 to 47.4% (95% CI = 31.52-63.28). As far as concerns crude numbers, most of the HAI were recorded in Medical wards (n = 37, 44.0%) and in Intensive Care Units (ICU) (n = 18, 21.4%), while the highest specific prevalence related to ward was recorded in ICU (47.4%, 95% CI = 31.52-63.28) and in Functional-Rehabilitation areas (20%, 95% CI = 8.31-31.69), followed by Hemato-Oncology (11.8%, 95% CI = 2.95-20.65) and Medical wards (8.5%, 95% CI = 5.89-11.12).

Even if numbers are limited when analyzed according to ward, a particular distribution of certain types of HAI, according to the various specific areas, clearly emerged: RTI (26.3%, 95% CI: 12.30-14.30) and BSI (13.2%, 95% CI: 2.44-23.96) were found to be the most prevalent localizations within the Intensive Care setting, while the same pattern emerged for UTI both in Functional-Rehabilitation areas (13.3%, 95% CI: 3.38-23.22) and in Medical wards (3.7, 95% CI: 1.93-5.47). A similar trend was observed for RTI (7.8%, 95% CI: 0.44-15.16) in Hemato-Oncological Units. Interestingly, 33.3% of the RTI diagnosed in ICU were Ventilation Associated Pneumonia (VAP).

Fig. 1. Relative frequency of Hospital Acquired Infections (HAI, n = 84) according to site.



UTI, urinary tract infections; RTI, respiratory tract infections; BSI, bloodstream infections; SSI, surgical site infections; GII, gastrointestinal infections; others, central nervous system infections, cardiovascular infections, eye infections, ear infections, infections of the reproductive system, unspecified infections

Tab. II. Prevalence of Hospital Acquired Infections (HAI), overall and according to site, referred to ward.

	UTI	RTI	BSI	SSI*	GII	Other Sites[a]	HAI Overall
	n (%, 95% CI)	n (%, 95% CI)	n (%, 95% CI)	n (%, 95% CI)	n (%, 95% CI)	n (%, 95% CI)	n (%, 95% CI)
General medicine and specialised medicine (n = 437)	16 (3.7, 1.93-5.47)	9 (2.1 , 0.76-3.44)	4 (0.9, 0.01-1.79)	1 (2.6, 0-7.59)	2 (0.5, 0-1.16)	5 (1.1, 0.12-2.08)	37 (8.5, 5.89-11.12)
General surgery and other specialised surgery (n = 193)	2 (1, 0-2.40)	- -	5 (2.6, 0.35-4.84)	1 (0.8, 0-2.37)	- -	1 (0.5, 0-1.50)	9 (4.7, 1.71-7.68)
Intensive care unit (n = 38)	1 (2.6, 0-7.66)	10 (26.3, 12.30-40.30)	5 (13.2, 2.44-23.96)	- -	1 (2.6, 0-7.66)	1 (2.6, 0-7.66)	18 (47.4, 31.52-63.28)
Hemato-onchology (n = 51)	- -	4 (7.8, 0.44-15.16)	2 (3.9, 0-9.21)	- -	- -	- -	6 (11.8, 2.95-20.65)
Obstetrics-gyneacology (n = 29)	- -	- -	- -	- -	- -	- -	0 -
Orthopaedics-thraumatology (n = 68)	1 (1.5, 0-4.39)	- -	- -	1 (1.6, 0-4.79)	- -	2 (2.9, 0-6.89)	4 (5.9, 0.3-11.5)
Otorinolaryngology (n = 4)	- -	- -	- -	- -	- -	- -	0 -
Oculistics (n = 6)	- -	- -	- -	- -	- -	1 (16.7, 0-46.54)	1 (16.7, 0-46.54)
Urology (n = 36)	- -	- -	- -	- -	- -	- -	0 -
Functional rehabilitation (n = 45)	6 (13.3, 3.38-23.22)	1 (2.2, 0-6.49)	2 (4.4, 0-10.39)	- -	- -	- -	9 (20, 8.31-31.69)
Neonatology (n = 5)	- -	- -	- -	- -	- -	- -	0 -

UTI, urinary tract infections; RTI, respiratory tract infections; BSI, bloodstream infections; SSI, surgical site infections; GII, gastrointestinal infections.
* Rates in surgical patients.
[a] Other sites: skin and connective tissue infections, bone and joint infections, central nervous system infections, cardiovascular infections, eye infections, ear infections, infections of the reproductive system, unspecified infections.

The specific prevalence of HAI diagnosed in Surgical Units was 4.7% (95% CI = 1.71-7.68): only one case could be attributed to SSI, while more than 50% of these infections were BSI (prevalence = 2.6%, 95% CI = 0.35-4.84).
Microbiological identification was available in 70 of the 84 infections (83.3%), while a total of 107 pathogens were isolated. HAI were sustained by a single and by two or more pathogens in 38 (54.3%) and 32 cases (45.7%), respectively. The most frequently found pathogens, overall and according to site of infection, are reported in Tables III and IV. The proportion of microbiologically confirmed HAI according to site was: 80.8% for UTI, 62.5% for RTI and 100% for BSI. In 11 UTI (42.3%), 7 RTI (29.2%) and 7 BSI (38.9%), two or more pathogens were isolated. In 7 of 18 BSI (38.9%) (5 Coagulase-negative *staphylococci* - CNS, 1 *Pseudomonas maltophilia* Multi Drug Resistant - MDR, and in 1 patient *Acinetobacter baumanii* Extended-Spectrum Beta-Lactamase – ESBL, and *Klebsiella pneumoniae* ESBL) and in 6 of 24 RTI (25%) (4 Methicillin-resistant *Staphylococcus aureus* - MRSA, 1 *Acinetobacter baumanii* ESBL and 1 *Pseudomonas aeruginosa* MDR) multidrug resistant pathogens were involved.
As far as concerns antibiotic use, 504 of the 912 patients (55.3%) monitored in the investigation received at least one dose during the study period. In particular, 291 patients (57.7%) received one antibiotic and 213 (42.3%) a combination of two or more. The indication for antimicrobial treatment was empirical therapy, prophylaxis and targeted therapy in 40.2%, 27.7% and 19.9%, respectively, while no information was available in the remaining prescriptions (12.2%).
The most frequently used antibacterial drugs were penicillin (26.7%), cephalosporins (22.8%), fluoroquinolones (17.9%) and aminoglycosides (5.3%): in particular, penicillin (26.4%), cephalosporins (19.3%) and quinolones (19%) being used primarily for empirical treatment, penicillin (37.4%) and cephalosporins (37.4%) for prophylaxis, and quinolones (20.6%) and penicillin (15.5%) for targeted therapy.

Tab. III. Leading pathogens in Hospital Acquired Infections (HAI).

Pathogens isolates (n= 107)	Number	(%)
Enterococcus spp.	18	16.8
Candida spp. (*C. albicans*)	15 (7)	14 (6.5)
Pseudomonas spp. (*P. aeruginosa*)	13 (9)	12.2 (8.4)
Staphylococcus aureus (MRSA)	13 (8)	12.2 (7.5)
Escherichia coli	11	10.3
Coagulase-negative *staphylococci*	10	9.3
Acinetobacter baumanni	6	5.6
Klebsiella spp.	5	4.7
Proteus spp.	3	2.8
Other	13	12.1

MRSA, Methicillin-resistant Staphylococcus aureus.

Discussion

The present results represent an update of the global epidemiological scenario of HAI in our Hospital, where the last wide survey was performed at the beginning of the nineties, with an overall prevalence of HAI of nearly 9% having been observed [15, 16].
If, on the one hand, some limits have been reported concerning the use of prevalence studies to accurately monitor the frequency of HAI, on the other, their rapidity, low cost and acceptable sustainability suggest this methodological approach to be a useful tool, and, in some instances, the only opportunity, to monitor this serious problem, in an active and systematic way, in large hospitals [5, 10, 17]. This is particularly the case in the present health-care institutions in which the rates of HAI are not routinely calculated, or are simply complitely unknown. The large number of inpatients monitored, the high bed-occupation rate, together with the appropriate use of an *ad hoc* protocol, in accordance with the international methods, definitions and criteria currently used, are all factors that add strength to our study.
In the present study, the prevalence of patients with HAI was similar to that reported in the broad survey performed in the Liguria region [10], and was also consistent with data reported by other authors, both in Italy and elsewhere in Europe, even in the high range [17-23]. In this respect, the decision to (i) cover most of the hospital settings, (ii) report all the infection types, and (iii) use a period- rather than a point-prevalence methodology

Tab. IV. Leading pathogens by site of infection.

Site of infection (pathogens isolated)	Pathogens isolated (%)	Pathogens isolated (%)	Pathogens isolated (%)	Pathogens isolated (%)	Pathogens isolated (%)
UTI (n = 33)	*Enterococcus* spp. (27.3)	*E. coli* (24.2)	*Candida* spp. (9.1)	Coagulase-negative *staphylococci* (6.1) *Citrobacter Freundii* (6.1) *Klebsiella* spp. (6.1) *Proteus* spp. (6.1)	Other (15)
RTI (n = 25)	*Pseudomonas* spp. (28)	*S. aureus* (24)	*Enterococcus* spp. (12)	*Candida* spp. (12)	Other (24)
BSI (n = 27)	Coagulase-negative *staphylococci* (25)	*Enterococcus* spp. (14.3)	*S. aureus* (10.7)	*Pseudomonas* spp. (10.7)	Other (39.3)

UTI, Urinary Tract Infections; RTI, Respiratory Tract Infections; BSI, Blood Stream Infections.

need to be considered. Moreover, an overstimation of the true frequency of certain HAI, due to the lack, by some investigators, of extensive clinical skills and experience, particularly required to distinguish contaminants from true pathogens, can not be excluded. However, it is well known that the frequency of HAI is usually higher in teaching, or in large-size, medical centers than in conventional or smaller institutions [17, 24-26]. Our hospital, as is well known, is the only University and reference adult acute-care center in the Liguria region, being, with its more than 1300 beds, one of the largest in Italy, as far as concerns an inpatient population. All these issues need to be taken into consideration when interpreting the results collected, particularly, for benchmarking purposes. Moreover, the relatively high mean age of the study population, together with the fact that nearly 80% of the patients enrolled were affected by at least one serious condition of co-morbidity, might further explain the high rate of HAI observed in the present study.

Since with evaluation only of the crude overall rate there is the risk of obscuring significant problems related to the specific HAI in particular settings [27-29], in this study frequencies according to site and speciality were also calculated. UTI and RTI were found to be the leading infections, these results being consistent with those published in several prevalence studies performed in Western Countries [10, 19, 21, 23-25, 27]. Interestingly, the highest specific prevalence of UTI was observed in long-term areas, such as Functional-Rehabilitation Units and Medical wards, both occupied primarily by elderly patients, frequently catheterized: these findings are also consistent with data reported in large prevalence investigations performed in other European Countries and in Italy [27, 30].

The low prevalence of HAI in Surgical Units, both overall and, in particular, those specific for SSI, could have been hardly biased by the shorter LOS following surgical interventions at our Hospital, due primarily to financial and organizational priorities. This would appear to suggest that a methodological approach other than prevalence (i.e., longitudinal studies), necessarily monitoring the occurrence of HAI during the post-discharge period, should be used for surveillance pourposes, as also indicated by other authors [17, 19, 27, 31-33].

BSI emerged as the third most frequent HAI in our Hospital, their prevalence (2.0%) being higher when compared both with that of the previously mentioned regional investigation in Liguria (1.5%) [10] and with the data recorded in other regional studies performed in Italy (range = 0.3-1.5) [17, 19, 27]. BSI are severe clinical pictures and are associated with high rates of mortality, particularly among elderly and critically ill patients, frequently institutionalized in high-risk settings [5, 34-36]. Moreover, BSI among immunocompromized patients can be sustained by opportunistic pathogens, as recently reported in our Hospital during an epidemic of *Ralstonia pickettii* bacteremia in patients with hematological malignancies and undergoing allogeneic hematopoietic stem cell transplant (HSCT) [37]. Assessment of the occurrence of BSI is widely recognised as a hospital indicator of the clinical performance: the fact that we found the highest prevalence of BSI and RTI in critical settings clearly shows that much effort is urgently needed to prevent these serious clinical pictures, starting from these high-risk areas. In this respect, the significant proportion (more than 30%) both of catheter-related bacteremia and VAP further highlights the need to review and share protocols concerning invasive procedures, in which the use of central vascular catheters (CVC) and respiratory medical devices are foreseen. The independent role of these invasive devices, in the risk of occurrence of HAI, has been clearly demonstrated in the literature [17, 38], also in the risk-assessment analysis in the recent investigation performed in our Region on a very large sample of the inpatient population [10]. Furthermore, greater efforts would appear to be necessary in our Hospital, at an organizational level, in order to reduce the LOS, which has also been demonstrated as an independent risk factor for all-type HAI occurrence [17, 18, 21, 38, 39].

With respect to the pattern of isolated pathogens, some considerations need to be made. If, on the one hand, our microbiological data are roughly in line with those reported in a large regional prevalence survey performed in North Eastern Italy [17], on the other, MRSA, as a proportion of *Staphylococcus aureus*, and CNS were found to be more frequently involved in HAI, in the present study, than in other similar large surveys performed during the last decade in Italy [19, 27]. Indeed, up to 25% of BSI were sustained by CNS, currently recognized as the leading pathogens associated with this type of infection [40, 41]. The emergence of these bacteria, usually resistant to multiple antibiotics, has been associated, for many years, with the increased use of intravascular devices, particularly CVC [28, 42-44]. Moreover, since a substantial prevalence of BSI (38.9%) and RTI (25%) sustained by multidrug resistant pathogens was found in the present study, all these findings further stress the need for prompt and appropriate corrective interventions.

Some final considerations on the use of antibiotics: the particularly high rate of administration of antibiotics found in the present study population (55.3%) clearly highlights the need for physicians to correctly follow the existing guidelines and recommendations, also in the view of the fact that exposure to antibiotics can represent an independent risk factor for HAI [17]: in addition to optimizing clinical management, this could lead to a reduction in the hospital antibiotic-resistant pattern, especially desirable in critical settings, with consequent improvements in terms both of quality and costs.

Results of the study provide an update of the epidemiological picture of HAI in our Hospital: even taking into the right account the above mentioned limitations, this knowledge has been already, and is currently, used as the scientific basis to planning and improving surveillance and control activities. The effectiveness of the corrective interventions adopted needs to be evaluated in the mid-term, i.e., by means of repeated prevalence investigations or, preferably, through longitudinal studies particularly in critical settings, depending on the available resources, both financial and in terms of full-time professionals within the hospital Infection Control Staff.

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■ List of abbreviations used

HAI: Hospital-Acquired Infections
LOS: Length of Hospital Stay
SAS: Statistical Analysis System
UTI: Urinary Tract Infection
RTI: Respiratory Tract Infection
BSI: Blood Stream Infection
ICU: Intensive Care Unit
VAP: Ventilation Associated Pneumonia
CNS: Coagulase-Negative Staphylococci
MDR: Multi Drug Resistant
ESBL: Extended-Spectrum Beta-Lactamase
MRSA: Methicillin-Resistant Staphylococcus Aureus
HSCT: Hematopoietic Stem Cell Transplant
CVC: Central Venous Catheter

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■ Authors' contributions

PD, MB, GO, PC, AB, CV and GI contributed to the conception and organization of the study. PD, MB, AB, GT, DB, AT and FD monitored the infections in the hospital wards. PD, MB, GO, AB, GT, CA, RI and GI contributed to acquisition, analysis and interpretation of data and were involved in drafting the manuscript. FD, FA, LS, DdF and CV gave final approval of the version of the manuscript to be published. PD and MB equally contributed in all the clinical and scientific activities performed in the study.

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