

Surveillance of healthcare acquired infections by “alert microorganisms”: preliminary results

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Key words: Cross infection, surveillance, healthcare acquired infection, multidrug resistant microorganisms

Parole chiave: Infezioni correlate all'assistenza, sorveglianza, microrganismi alert

Abstract

Background. We evaluated the trend of four years (2015 – 2018) of “alert organisms” surveillance carried out at the 450 bed teaching hospital S. Andrea in Rome.

Methods. All patients with an “Alert organism” isolation were screened. In accordance with definitions used by the Centers for Disease Control patients with an “alert organism” isolation were evaluated for infection or colonization, by an infection control team (ICT).

Results. Between April 2015 and December 2018 a total 4,762 specimens with “Alert organism” isolation were screened and 1,601 patients were surveyed and included in the study. Overall 780 (48.8%) patients developed an healthcare acquired infection (HAI) at our institution, whereas 311 (19.4%) entered with a community acquired infection, 254 (15.8%) with an infection acquired in another healthcare setting and 256 (16.0%) resulted simply colonized. The 780 patients who developed an HAI at our institution presented 878 infectious episodes and the isolation of 931 microorganisms. *C. difficile* infections were the most common (27.2%), followed by 21.3% respiratory tract infections, 16.9% urinary tract infections, 15.5% surgical site infections, 12.5% bloodstream infections, 3.6% ulcers and 3.0% others. Among HAI group Gram negatives (54.1%) were more frequent than Gram positives (45.9%), whereas in patients entering in the hospital already with a community infection Gram positives overpassed Gram negatives (58.7% vs. 41.3%; $p < 0.001$). Most common pathogens responsible for HAI were *C. difficile* (25.6%), *Klebsiella* spp. (25.5%), MRSA (19.6%) and *Acinetobacter* spp. (15.3%). Notably 30.0% HAI at other institutions were represented by *C. difficile*. Impressively, >40% of community acquired infections were related to MRSA.

Conclusions. The present study provided some useful insight into the major multi-resistant pathogens epidemiology at our institution. The Authors succeeded in organizing a multidisciplinary ICT that created a partnership feeling with the hospital personnel.

Introduction

Surveillance is an essential component of any comprehensive infection control program to contrast Healthcare acquired infections (HAI) and their costs (1).

Already 40 years ago, the importance of surveillance was demonstrated by the Study on the Efficacy of Nosocomial Infection control (SENIC), which found a 32% reduction in nosocomial infections in hospitals with active surveillance

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programs compared with hospitals without such programs (2).

Also it is well recognized that factors such as individual patients susceptibility, invasive devices, inadequate hand hygiene guidelines respect (3), poor ward hygienic conditions (4), obsolete water supply systems (5-6), inappropriate and prolonged antibiotics use (7) increase the HAIs incidence (8).

The first aim of surveillance is to determine infection rates, main infection sites, common microorganisms, and the use of antibiotics, as appropriate empiric therapy is considered to be the most important factor for patients outcome. For this reason it is important to know the pathogens causing infection and their antimicrobial resistance pattern to guide appropriate antimicrobial treatment (7-9).

In particular the rising multidrug resistance has an impact on patients, showing higher mortality and frequent treatment failure among them compared with those infected with the susceptible isolates (10-11).

Unfortunately the epidemiology and antimicrobial profile of microorganisms responsible for HAI varies between institutions, and within the hospital wards. Also, as the rates of antimicrobial resistance in pathogens principally among Gram-negatives are increasing, every center should be familiar with its local trends in order to target a more appropriate empirical therapy (12-13).

Therefore, in order to better understand the local HAI epidemiology and to implement infection control programs, we evaluated the trend of four years (2015 – 2018) of “alert organisms” surveillance carried out at the teaching hospital S. Andrea in Rome.

Materials and Methods

Setting

The study was carried out in the 450 bed Teaching Hospital “Sant’Andrea” in Rome,

Italy, where the annual HAI prevalence was 6.34% (14). We developed an “Alert organisms” surveillance system, which included Microbiology Laboratory, Hospital Hygiene unit and Infectious Diseases Unit. Every day when the Microbiology Laboratory isolated a pathogen included in the “Alert organisms” list an automatic notification was sent to the Hospital Hygiene unit where an infection control nurse visited the ward and reviewed clinical charts. Also infectious disease physicians were involved.

An alert list, based on national and international scientific societies guidelines and recommendations (8) was determined by an interdisciplinary team which integrated these suggestions with teaching hospital specific requests.

Surveillance included the following “Alert organisms”:

- methicillin resistant *Staphylococcus aureus* (MRSA);
- Vancomycin resistant enterococci (VRE);
- Multidrug resistant *Acinetobacter baumannii* (MDR-A. *baumannii*);
- Multidrug resistant *Pseudomonas aeruginosa* (MDR-P. *aeruginosa*);
- Carbapenem resistant enterobacteriaceae;
- *Clostridium difficile*;

Definition

From April 2015 to December 2018 all patients with an “Alert organism” isolation were screened. In accordance with definitions used by the Centers for Disease Control (15) patients with an alert organism isolation were evaluated for infection or colonization. All infections occurring more than 48 hours after hospital admission were considered HAI, when patient were admitted to hospital directly from another healthcare setting they were considered HAI from another hospital. All the rest were community infections. If the same microorganisms had been isolated

more than once in the same patient only one was included in the analysis.

Data Collection

Data from clinical and microbiological records were collected by an infection control team (ICT) composed by an infection control nurse and two infectious diseases physicians, using a specially designed form.

The following information was recorded: demographic characteristics (i.e. sex, age...), unit of admission, date of admission, kind of specimen, date of collection, date of infection, risk factors, infection characteristics. All isolated microorganisms and their antibiotic susceptibility were screened and recorded.

All data were coded and entered into a PC for statistical analysis using a specific database oriented software (Epi-Info version 2012, CDC).

Microbiological methods

All patient samples were taken for culture according to the general principles of specimen collection and transport (16). The species identification and the antimicrobial susceptibility testing were performed on the isolated strains by using the MALDI-ToF system (Microflex LT system; Bruker Daltonics, Italy) and Phoenix BD system, respectively. A phenotypic confirmation test of carbapenemase production in Enterobacteriaceae isolates having a minimum inhibitory concentration >0.5 $\mu\text{g}/\text{mL}$ for meropenem and/or imipenem. Carbapenemase production was confirmed by Hodge-Test modified and after by disc diffusion synergy test including meropenem and two carbapenemase inhibiting compounds (dipicolinic acid and boronic acid) (17). Breakpoints were interpreted in accordance with the European Committee on Antimicrobial Susceptibility Testing guidelines (18-19). In case of controversial or difficult to interpret results, a IVD PCR-based method able to differentiate IMP1, VIM, NMD, KPC and OXA 48 classes

produced by CRE isolates were employed (GeneExpert system, Cepheid AB, Solna, Sweden).

Among microorganisms the multi-drug resistance (MDR) was defined according to the ECDC guidelines (20).

Data Analysis

Statistical analyses were performed using Epi-Info (Epi-Info version 2012, CDC). The chi-square was used to examine differences between groups. Statistical significance was defined as a P value of less than 0.05. The univariate relationship between infection and death was tested using relative risk and its 95% confidence interval (CI_{95}).

Results

A total 4,762 specimens with “Alert organism” isolation were screened by the microbiology laboratory during the study period.

Consequently, between April 2015 and December 2018, 1,601 patients were surveyed and included in the study. Overall 780 patients developed an healthcare acquired infection (HAI) at our institution, whereas 311 entered with a community acquired infection, 254 with an infection acquired in another healthcare setting and 256 resulted simply colonized after scrupulous medical evaluation. Table 1 shows the distribution of all types of infections due to “alert organisms” in the hospital wards. Over 80% of surveyed patients had an infection as only 16.0% resulted colonized. However, about 1/3 of patients entered the hospital with an infection acquired either in the community (19.4%) or in another healthcare setting (15.8%). In some hospital wards this phenomenon affected $>50\%$ of surveyed patients.

Among patients with HAI acquired at our institution 57.8% were males and 42.2% females. A total 317 (40.7%) patients

Table 1 - Patients distribution by infection status and hospital ward

Ward	HAI		HAI other setting		Community infections		Colonization		Total	
	Isolates	%	Isolates	%	Isolates	%	Isolates	%	Isolates	%
Medical wards	428	54.9	189	74.8	246	79.1	164	64.1	1027	64.1
Surgical wards	239	30.6	32	12.6	41	13.2	50	19.5	362	22.7
Intensive Care	113	14.5	32	12.6	24	7.7	42	16.4	211	13.2
Total	780	100.0	253	100.0	311	100.0	256	100.0	1601	100.0

underwent surgery, 603 (77.3%) urinary catheterization, 270 (34.6%) mechanical ventilation, 172 (22.1%) PICC and 56 (7.2%) central venous catheterization. The onset of infection in patients followed hospital admission by 12.5 ± 14.3 (mean) and 13 days (median).

The 780 patients who developed an HAI at our institution presented 878 infectious episodes and the isolation of 931 microorganisms. *C. difficile* infections were the most common (27.2%), followed by 21.3% respiratory tract infections (RTIs), 16.9% urinary tract infections (UTI), 15.5% surgical site infections (SSI), 12.5% bloodstream infections (BSI), 3.6% ulcers and 3.0% others (Table 2).

Almost 1/3 of infectious episodes acquired at another healthcare setting in patient subsequently admitted to the teaching hospital were due to *C. difficile* (32.5%).

Whereas among community acquired the main infection was represented by RTIs (29.9%) (Table 2).

Table 3 shows the distribution of “alert organisms” responsible for infectious episodes during the study period. Among HAI group Gram negatives (54.1%) were more frequent than Gram positives (45.9%), whereas in patients entering in the hospital already with a community infection Gram positives overpassed Gram negatives (58.7% vs. 41.3%; $p < 0.001$). The most common pathogens responsible for HAI were *C. difficile* 43 (25.6%), *Klebsiella* spp. (25.5%), MRSA (19.6%) and *Acinetobacter* spp. (15.3%). Notably 30.0% of HAI at other institutions were represented by *C. difficile*. Impressively, MRSA was significantly more frequent in community acquired infections compared to HAIs (40.5% vs. 19.5%; $p < 0.001$).

Overall, *C. difficile* was the single most

Table 2 - Infectious episodes distribution among patients with HAI

Microorganism	HAI		HAI from other setting		Community acquired infection		Total	
	Isolates	%	Isolates	%	Isolates	%	Isolates	%
<i>C. difficile</i> infection (CDI)	239	27.2	93	32.5	62	18.3	394	26.3
Respiratory tract infections	187	21.3	58	20.3	101	29.9	346	23.0
Urinary tract infections	148	16.9	29	10.1	50	14.8	227	15.1
Surgical site infections	136	15.5	36	12.6	26	7.7	198	13.2
Bloodstream infection	110	12.5	29	10.1	20	5.9	159	10.6
Ulcers	32	3.6	29	10.1	36	10.6	97	6.5
Other	26	3.0	12	4.2	43	12.7	64	4.3
Total	878	100.0	286	100.0	338	100.0	1502	100.0

Table 3 - Distribution of “alert microorganisms” responsible for infectious episodes

Microorganism	HAI		HAI other setting		Community infections		Total	
	Isolates	%	Isolates	%	Isolates	%	Isolates	%
MRSA ^	182	19.5	79	25.5	147	40.5	408	25.4
<i>C. difficile</i>	238	25.6	93	30.0	63	17.4	394	24.6
Enterococcus spp.	7	0.7	1	0.3	3	0.8	11	0.7
Total Gram+	427	45.9	173	55.8	213	58.7	813	50.7
<i>A. baumannii</i>	113	12.1	54	17.4	35	9.6	224	14.0
Acinetobacter spp.	29	3.1	7	2.3	5	1.4	20	1.2
<i>E. coli</i> †	22	2.4	6	1.9	11	3.0	39	2.4
Klebsiella pneumoniae †	197	21.2	43	13.9	52	14.3	291	18.1
Klebsiella spp. †	41	4.4	7	2.3	13	3.6	61	3.8
Pseudomonas spp.	15	1.6	3	1.0	4	1.1	22	1.4
<i>P. aeruginosa</i>	80	8.6	16	5.2	30	8.3	126	7.9
Other Gram-	7	0.7	1	0.3	0	-	8	0.5
Total Gram-	504	54.1	137	44.2	150	41.3	791	49.3
TOTAL	931	100.0	310	100.0	363	100.0	1604	100.0

^ Methicillin resistant *S. aureus*; † Enterobacteriaceae Carbapenem resistant;

frequently isolated microorganism (Table 4). The aetiologic agents principally responsible for respiratory tract infections were MRSA (33.0%) followed by *Klebsiella* spp. (26.4%) and *Acinetobacter* spp. (25.0%). Gram negatives caused the vast majority of urinary tract infections (>90%), and were responsible for most surgical site infections (>70%). MRSA was the single most frequent microorganism responsible for bloodstream infection (38.1%), although Gram negatives (61.1%) overtook Gram positives (38.9%) (Table 4).

Discussion

Although the present surveillance did not include all HAIs, investigating only “alert organisms” onset and distribution (multidrug resistant organisms and *C. difficile*), in our opinion these preliminary results could offer some interesting and useful indications.

Many studies have been carried out on multidrug resistant HAIs (7, 8, 12, 13, 21), however knowledge on local patterns can aid

clinicians in their decision making processes, resulting in improved quality of care. Therefore we decided to perform an epidemiological study in order to assess more detailed data on the circulating aetiology at our institution, and provide baseline data for rational control and prevention activities (22).

The main purpose of surveillance on HAI is to detect shifts in the involved bacteria in order to help improving the choice of empiric therapy. The strength of such studies relies on clear and standardized clinical diagnostic criteria which make data reliable and realistic, avoiding confounding colonizing agents not directly related to clinical disease (as it may occur when ventilator associated pneumonia are considered).

Calfee et al. (23) showed how healthcare management changes may cause a false modification of nosocomial infection rates. In our study the infection control team staff carrying out the infection diagnosis remained the same during all the study period.

The study included over 1,600 patients admitted to the teaching hospital with isolation of an “alert” organism. When

Table 4 - Distribution of “alert microorganisms” responsible for HAI

Microorganism	C. difficile infection		Respiratory tract infections		Urinary tract infections		Surgical site infections		Bloodstream infections		Ulcers		Others		Total	
	Isolates	%	Isolates	%	Isolates	%	Isolates	%	Isolates	%	Isolates	%	Isolates	%	Isolates	%
MRSA ^	0	-	70	33.0	7	4.5	42	28.6	43	38.4	15	42.9	5	18.5	182	19.5
<i>C. difficile</i>	238	-	0	0	0	0	0	-	0	-	0	-	0	-	238	25.7
<i>Enterococcus</i> spp.	0	-	2	0.9	4	2.5	0	-	1	0.9	0	-	0	-	7	0.7
Total Gram+	238	100	72	34.0	11	7.0	42	28.6	44	39.9	15	42.9	5	18.5	427	45.9
<i>A. baumannii</i>	0	-	40	18.9	14	8.9	23	15.6	20	16.9	10	28.6	6	22.2	113	12.1
<i>Acinetobacter</i> spp.	0	-	13	6.13	4	2.5	10	6.8	0	-	0	-	2	7.4	29	3.1
<i>E. coli</i> †	0	-	3	1.4	10	6.4	7	4.8	2	1.8	0	-	0	-	22	2.4
<i>Klebsiella pneumoniae</i> †	0	-	41	19.3	82	52.3	27	18.4	33	29.5	6	17.1	7	25.9	197	21.2
<i>Klebsiella</i> spp. †	0	-	15	7.1	10	6.4	8	5.4	6	5.4	1	2.9	1	3.7	41	4.4
<i>Pseudomonas</i> spp.	0	-	4	1.9	4	2.5	6	4.1	1	0.9	0	-	0	-	15	1.6
<i>P. aeruginosa</i>	0	-	19	9.0	22	14.0	23	15.6	6	5.4	3	8.6	6	22.2	80	8.6
Other Gram-	0	-	5	2.4	0	0	1	0.7	1	0.9	0	-	0	-	7	0.7
Total Gram-	0	-	140	66.0	146	93.0	105	71.4	69	61.6	20	57.1	22	81.5	504	54.1
TOTAL	238	100.0	212	100.0	157	100.0	147	100.0	113	100.0	35	100.0	27	100.0	931	100.0

^ Methicillin resistant *S. aureus*; † Enterobacteriaceae;

considering HAI origin we noticed that 564 (42.0%) patients out of 1,344 were admitted in the teaching hospital already with an “alert organisms” infection Table 1. These patients were mostly admitted to the medical wards (>75%), whereas many less in the surgical units (<15%).

Surveillance showed that *C. difficile* infections were the most frequently acquired at our hospital or in other healthcare settings (30%) Table 2. The epidemiology of *C. difficile* is constantly changing and is influenced by antibiotic usage patterns, healthcare patient environment and emergence of new strains (24). Therefore ongoing specific surveillance will be important to track the ever-changing epidemiology of this remarkably adaptable pathogen.

Differently, in the community the most frequent acquired infections were RTIs (29.9%).

HAIs were predominantly caused by Gram-negative microorganisms, particularly *Klebsiella* spp. (>25%). Although resistance rates vary widely according to the individual hospital, city or country involved, MDR *Klebsiella* spp. have been reported increasingly world wide (7), as in our institution. The ability of these microorganisms to develop resistance to multiple antibiotics increases the chances for inappropriate empiric therapy, which has been shown to be an independent risk factor for adverse outcome (21). Among gram-negative nonfermenters the two most frequently isolated pathogens responsible for HAIs were *A. baumannii* and *P. aeruginosa*.

Secondly to *C. difficile*, MRSA represented the main multidrug resistant Gram-positive responsible for HAI, whereas vancomycin resistant enterococci were marginal.

It was impressive that MRSA was responsible for >40% of community acquired infections, showing a vast circulation of resistant organisms in the community.

Traditionally MRSA are considered a

healthcare-associated pathogen in hospital patients, with well described risk factors. However, in the last decade serious infections have been isolated with increasing frequency in community patients without established risk factor (25-26). Community acquired MRSA infections represent a major cause of concern for physicians, who must consider this microbial aetiology not only in cases of nosocomial acquisition but also in patients coming from the community without any risk factors for MRSA colonization or infection. Clinicians should recognize, on the basis of the presence of specific risk factors, those patients who have a high likelihood of infection due to these microorganisms. Therefore population based studies on MRSA prevalence in the community and interaction with hospitals is needed.

Almost 30% of microorganisms responsible for community acquired infections were represented by *Klebsiella* and *Acinetobacter*, indicating a strong circulation of these MDR Gram-negatives out of the hospital environment.

The study results on “alert” organisms confirm an alarming circulation of antimicrobial resistant bacteria which raises global concerns regarding the impact on patients with MDR infections, which are expected to be more costly for healthcare systems than susceptible ones, as they cause a higher length of stay in the hospital (9, 12, 13, 27-30). Also these multiresistant infections put greater difficulties in prevention (8, 31).

We are aware of some limitations to our study. First it was carried out in a single center, secondly the data were collected for the purposes of infection control surveillance and consequently some clinical information may were limited, third mortality was not always reported.

However the study adopted a clear and standardized clinical diagnostic criteria which avoided confounding colonizing agents not directly related to clinical disease, excluding specimen duplicates was

important, as inclusion of duplicates can result in overestimation of some microorganisms. Data was collected prospectively by an infection control team using the same methodology along all the study period and, in order to improve surveillance data comparison, ECDC MDR standard definitions were adopted (20).

Conclusions

The present study provided some useful insight into the major multi-resistant pathogens epidemiology at our institution.

Our results underline the importance of surveillance, particularly of MDR organisms which add significantly to mortality. Since early appropriate empirical treatment improves survival in patients affected by serious infections, specific studies are needed to identify risk factors for MDR organisms isolation in ICU patients.

The Authors succeeded in organizing a multidisciplinary ICT that created a partnership feeling with the hospital personnel.

Riassunto

Sorveglianza delle infezioni correlate all'assistenza da “microorganismi alert”: risultati preliminari

Introduzione. È stato condotto uno studio sulla sorveglianza delle infezioni correlate all'assistenza (ICA) da microorganismi “alert” presso l'ospedale universitario Sant'Andrea di Roma (450 posti letto).

Metodi. Da Aprile 2015 a Dicembre 2018 i pazienti con isolamento di un microorganismo “alert” sono stati valutati. Applicando le definizioni di caso secondo i CDC, lo studio ha considerato i vari tipi d'infezione. L'identificazione di specie è avvenuta mediante sistema Maldi-Tof (Bruker) e la resistenza è stata valutata con il sistema Phoenix BD, secondo le linee guida della European Antimicrobial Resistance Surveillance System (EARSS).

Risultati. Sono stati isolati 4.762 campioni microbiologici e 1.601 pazienti sono stati inclusi nello studio. In totale 780 (48.8%) pazienti hanno sviluppato un'ICA presso il nostro ospedale, 311 (19.4%) un'infezione co-

munitaria, 254 (15.8%) un’ICA presso un’altra struttura sanitaria e 256 (16.0%) sono risultati semplicemente colonizzati. Nei 780 pazienti che hanno sviluppato un’ICA presso il nostro ospedale si sono verificati 878 episodi infettivi causati da 931 microrganismi. Le infezioni da *C. difficile* (27,2%) sono state le più comuni, seguite dalle infezioni delle vie respiratorie (21,3%), vie urinarie (16,9%) sito chirurgico (15,5%), setticemie (12,5%), ulcere (3,6%), ed altro (3,0%). Nelle ICA acquisite presso il nostro ospedale i Gram-negativi (54,1%) erano più frequenti dei Gram-positivi (45,9%), mentre nei pazienti con infezioni comunitarie i Gram-positivi superavano nettamente i Gram-negativi (58.7% vs. 41.3%; $p < 0.001$). I patogeni più spesso responsabili delle ICA acquisite presso il nostro ospedale sono stati *C. difficile* (25,6%), *Klebsiella* spp. (25,5%), MRSA (19,6%) ed *Acinetobacter* spp. (15,3%). Da notare che il 30,0% delle ICA acquisite presso un’altra struttura sanitaria era rappresentato da *C. difficile*. Nelle infezioni comunitarie >40% delle eziologie era da MRSA.

Conclusioni. La sorveglianza è indispensabile per conoscere l’epidemiologia dei microrganismi responsabili delle ICA e modulare le politiche di prevenzione più efficaci.

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