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Mortality rate and length of stay due to hospital acquired infections in a metropolitan hospital in Sicily

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ABSTRACT:

— ***Background:*** Hospital-acquired infections (HAIs) can be considered the most frequent adverse event threatening the life of patients. HAIs, added to the underlying disease, increase morbidity and mortality and have a considerable economic impact. This study aims at evaluating the prevalence of HAIs in a metropolitan hospital, to identify the risk factors and to assess the potential clinical implication.

— ***Patients and Methods:*** This is a retrospective observational study conducted in Catania, Italy. Demographic, epidemiological and clinical data were recorded for each patient with at least one available bacterial culture, hospitalized in the period from March 2005 to April 2010. HAIs were identified and classified according to the CDC/NHSN criteria. Mortality and duration of hospital stay were considered an outcome. The Chi-squared test and odds ratio were used for nominal variables, the Chi-squared test for trend was used to evaluate the trend of percentages over time.

— ***Results****:* 599 positive cultures were identified from 372 patients. In 216 (58%) patients we observed at least a HAI: 149 (40%) developed a single HAI, 67 (18%) developed more than one HAI. 300 HAIs were identified: 170 lung infections, 102 blood stream infections. The risk of infection was greater for patients with invasive devices. The probability of death in the presence of HAI was 52.9%. The mortality rate increased with age, comorbidity and number of HAIs. The development of an HAI by *A. baumannii* was an important risk factor for death during hospitalization. HAIs were associated with prolonged length of stay.
Conclusions: In this study we found that HAIs play a critical role in patients' management, length of stay, mortality, and augmented hospitalization cost.

— ***Key words:*** Bacterial infection, Hospital acquired infections (HAI), ICU, Length of stay.

INTRODUCTION

Hospital-acquired infections (HAIs) can be considered the most frequent adverse event occurring to hospitalized patients and significantly increasing morbidity and mortality[1].

While in developed countries the number of patients treated in hospitals and the average length of stay have decreased during recent decades, HAIs have increased. In addition, the consequences of HAIs have become more severe than a decade ago, because of the increasing number of highly vulnerable patients along with the emergence of antibiotic resistant microbes. In fact, decreased host defenses, mucosal colonization by pathogenic microorganisms and the disruption of the integrity of the skin surface, caused by implantable medical devices, contribute to the development of HAIs[1,2].

HAIs result in a considerable economic damage due to the increased use of drugs, the need for isolation, the wider use of laboratory and instrumental tests, the increase in inpatient days, the loss of days of work. As a matter of fact, in 2000, the US Centers for Disease Control and Prevention estimated the total costs of nosocomial infections to be in excess of 5 billion US$. These numbers do not take in account the vast cost of treating these infections and disabilities caused by them.

Thus, it becomes very important to assess the epidemiology of HAIs in terms of antimicrobial resistance profile and risk factors, in order to intervene in a targeted fashion.

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This study aims to evaluate the prevalence of HAIs in some hospital wards of a metropolitan hospital in Sicily, to identify risk factors and to assess their impact on clinical outcomes.

PATIENTS AND METHODS

This is a retrospective observational study that was conducted in 4 wards of the "Garibaldi Nesima" Hospital in Catania, Southern Italy, a large metropolitan hospital with 437 beds: Anesthesia and Intensive Care (ICU) (6 mixed type beds, operating since 2004), Infectious Diseases (20 beds, operating since 2005), Nephrology (13 beds, operating since 2005), and Medical Oncology (20 beds, operating since 2005).

To obtain demographic, epidemiological and clinical data, we examined the medical records of patients having at least one bacterial culture from bronchial aspirates, blood, catheter, cannulae and prosthesis, with a positive result for *Staphylococcus (S.) aureus*, coagulase-negative Staphylococchi (CoNS), *Acinetobacter (A.) baumannii, Pseudomonas (P.) aeruginosa, Escherichia (E.) coli, Enterobacter (E.) cloacae, Klebsiella (K.) pneumoniae, Enterococcus (E.) faecalis* and *E. faecium*, in the period from March 2005 to April 2010.

HAIs were identified and classified according to the CDC/NHSN criteria[3].

For each HAI only one isolate has been included in the study. In case of polymicrobial infections, each isolate was separately included in the database. Patients with urinary tract infections were excluded from the study.

Mortality was the outcome of interest if the patient died during hospitalization, whereas the duration of hospital stay was the outcome in case of discharge.

The Charlson Comorbidity Index (CCI) was used to determine the impact of comorbidities.

Statistical significance was defined as $p < 0.05$. The Chi-squared test and odds ratio (OR) were used for nominal variables, the Chi-squared test for trend was used to evaluate the trend of the percentages over time.

RESULTS

599 positive cultures were retrospectively identified on samples from 372 patients. HAI prevalence and their distribution by ward and by etiology are shown in Table 1 and Table 2, respectively.

The probability of death in the presence of HAI was 52.9%.

In 216 (58%) patients, we observed at least one HAI: 149 (40%) developed one HAI, 50 (13.4%) developed 2 HAIs, 16 (4.3%) developed 3 HAIs, 1 patient developed 4 HAIs.

On the other hand, colonization was observed in 156 patients: 80% of patients admitted to the Infectious Diseases ward, 57.1% of those admitted to the Nephrology one, 32.2% of those in Medical Oncology and 31.6% of those admitted to the ICU.

For colonized patients, the mortality rate was 19.2%, while among patients with HAIs the mortality rate ranged from 39.2% for those who developed one HAI to 52.9% for those who developed more than 2 HAIs ($p < 0.0001$) (Figure 1).

The median length of hospital stay was 10 days for patients with contamination, 21 for patients with a single HAI, 34 for those with 2 HAIs and 55 days for those with more than 2 HAIs (Figure 2).

287 (77%) patients had implanted invasive devices, including all patients admitted to the ICU, 86% of those admitted to Nephrology, 58% of those in Medical Oncology and 5% of those in Infectious Diseases.

300 HAIs were identified and classified: 250 (83.3%) in patients admitted to the ICU, 25 (8.3%) in patients admitted in the Medical Oncology ward, 20 (6.6%) in patients admitted in the Infectious Diseases unit and 5 (1.7%) in patients admitted to the Nephrology ward.

170 patients had lung infections: 141 ventilator associated pneumonias (VAP), representing 46.6% of all HAIs, and 29 pneumonia (PNEU) (9.6%). The prevalence of respiratory tract infections (74.4%) was higher in the ICU. 102 (34%) had laboratory-confirmed bloodstream infections (LCBSI), of whom 75 were central-line

Table 1. HAI prevalence in the different Units involved in the study.

HAI	Infectious diseases		Nefrology		Medical oncology		ICU	
N	%	N	%	N	%	N	%	
BRON	0	0	0	0	0	0	15	6
CLABSI	4	25	2	40	11	44	58	23.2
GIT	0	0	0	0	0	0	1	0.4
IAB	0	0	0	0	1	4	1	0.4
LCBI	14	70	1	20	12	48	0	0
MEN	0	0	0	0	0	0	1	0.4
PNEU	2	10	2	40	0	0	25	10
SSI	0	0	0	0	1	4	3	1.2
UR	0	0	0	0	0	0	5	2
VAP	0	0	0	0	0	0	141	56.4
N	20	100	5	100	25	100	250	100

Table 2. HAI prevalence according to the microbiological isolate.

Bacterialspecies	BRON		CLABSI		LCBI		PNEU		VAP		SSI		GIT		IAB		MEN		UR	
	Tot	%	Tot	%	Tot	%	Tot	%	Tot	%	Tot	%	Tot	%	Tot	%	Tot	%	Tot	%
A. baumannii	4	26.67	11	14.66	0	0	4	13.8	39	27.66	0	0	0	0	0	0	1	100	1	20
E. cloacae	2	13.33	17	22.66	1	3.7	0	0	4	2.84	1	25	0	0	0	0	0	0	1	20
E. faecalis	0	0	5	6.66	0	0	0	0	4	2.84	0	0	0	0	0	0	0	0	1	20
E. faecium	0	0	0	0	0	0	1	3.4	5	3.55	0	0	0	0	0	0	0	0	0	0
E. coli	0	0	4	5.33	8	29.63	6	20.7	5	3.55	1	25	0	0	0	0	0	0	0	0
K. pneumoniae	1	6.67	2	2.66	1	3.7	2	6.9	5	3.55	0	0	0	0	0	0	0	0	0	0
P. aeruginosa	4	26.67	6	8	4	14.81	9	34.5	56	39.72	2	50	1	100	1	100	0	0	2	40
S. aureus	3	20	6	8	3	11.11	3	10.3	10	7.09	0	0	0	0	0	0	0	0	0	0
CONS	1	6.67	21	28	10	37.03	2	10.3	13	9.22	0	0	0	0	0	0	0	0	0	0

associated (CSA) BSI. The proportion of positive isolates that was associated with HAI was higher in Medical Oncology (71.4%), followed by ICU (53%), Nephrology (50%) and Infectious Diseases (23.5%).

CoNS were the cause of 100% of CLABSI and 60% of LCBI in the Infectious Diseases ward, 50% of CLABSI in the Nephrology ward, of 45.5% of those in Medical Oncology and of 25.5% of those in ICU.

E. cloacae (27.3%) and *A. baumannii* (20%) were also responsible for CLABSI in the ICU.

E. coli was isolated in 10% of patients with LCBSI in the Infectious Diseases ward, 100% of them in Nephrology and in 50% of them in Medical Oncology.

P. aeruginosa caused 42.8% of PNEU observed in ICU and 50% of those observed in Nephrology.

PATIENTS STRATIFIED BY NUMBER OF POSITIVE CULTURES

The patients were then divided into two groups according to the number of culture with positive results: group 1, patients with a single bacterial isolate (239 patients, 64%); group 2, patients with two or more bacterial isolates (131 patients, 36%).

Group 1: patients with a single bacterial isolation

43.5% of patients in group 1 developed an HAI. The mortality rate among patients who developed an HAI was 42.3%, while among those with contamination was 18.5% (OR 3.23). For women, the mortality rate was 41.2% in case of HAI *vs.* 11.7% for contamination (OR 5.05); in males, the mortality rate were 42.9% and 24%, respectively (OR 2.34).

Figure 3 shows the proportion of isolates that resulted in a HAI. *A. baumannii* was isolated in 30 patients in this group and was responsible for HAIs in 63% of cases. *E. cloacae* isolates were associated with HAI in 44% of cases, Enterococcus *spp* in 42%, *E. coli* in 51%, *K. pneumonia* in 42%, *P. aeruginosa* in 63%, *S. aureus* in 23% and CoNS in 28%.

Figure 4 shows the mortality rate of patients who developed an HAI *vs.* contamination, stratified for bacterial species.

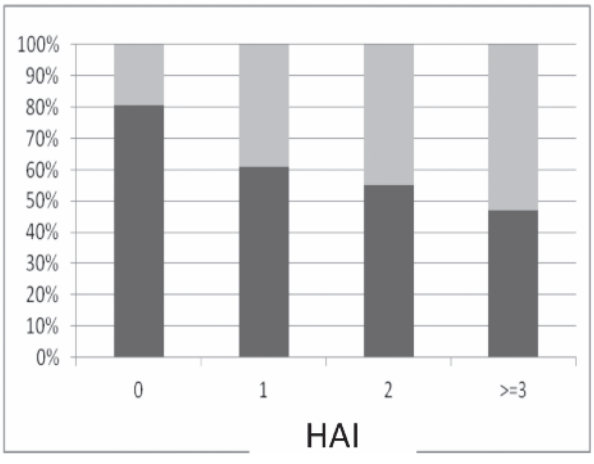

Figure 1. Distribution of patients who died (light gray) or were discharged (dark gray) according to the number of HAIs.

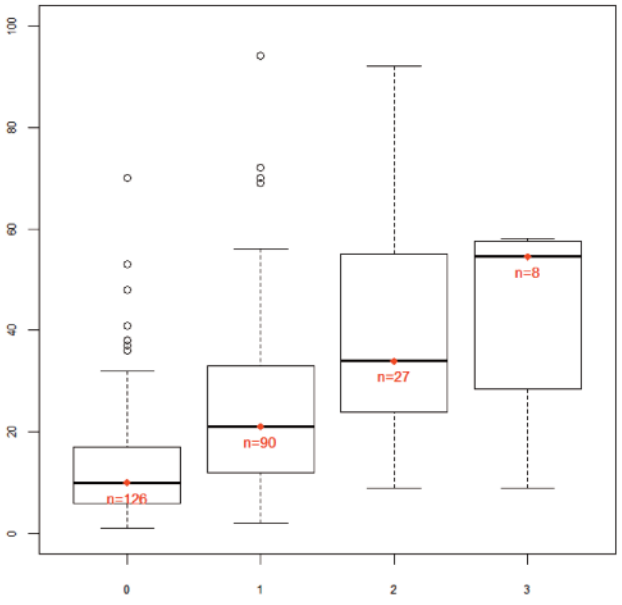

Figure 2. Median length of hospital stay according to the number of HAIs.

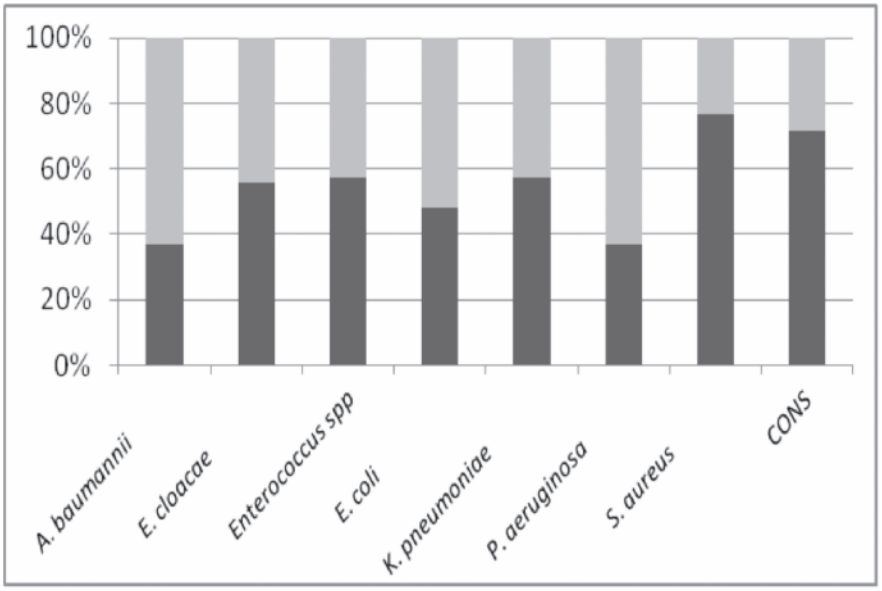

Figure 3. Infectivity rate among patients with one positive culture according to the bacterial isolate. Light gray: HAI; dark gray: colonization

When stratified by type of HAI, the patients with a single positive culture, presented the following mortality rate: PNEU: none of the patients who developed a PNEU died during hospitalization; LCBI: 21.7%; VAP: 47.9%, CLABSI: 58.8%, other HAI (BRON, IAB and UR): overall 85.7%.

Patients who experienced an HAI during admission had a mortality rate of 16.7% if aged between 0 to 30 years, while none of the patients in this subgroup with just contamination died (OR 5,18), of 33.3% if aged between 30 to 50 years (while 12.5% among those with just contamination: OR 3.5), of 34.1% if aged between 50 to 70 years (18.8% among those with just contamination: OR 2.25) and of 59% if were over 70 years (26.1% among those with just contamination: OR 4.07).

Table 3 shows, stratified by ward, the mortality rate of patients who developed a HAI *vs.* those with contamination.

52.9% of patients with an implanted invasive device developed an HAI *vs.* 25.6% of those without implanted device (OR 3.26, $p < 0.0001$). Patients with a HAI and an invasive device had a mortality rate of 48.2% *vs.* 19% of those without device (OR 3.95).

9.1% of patients without comorbidities (CCI=0) developed an HAI; 40.5% of patients with CCI=1 developed an HAI, 47.2% of those with CCI=2, 60% of those with CCI equal to 3 or 4 and 45.2% of those with CCI=5. Among patients with CCI=0, the mortality rate was 66.7% among those who developed an HAI and 6.7% among those with colonization (OR 28, $p = 0.0024$). In patients with CCI=1, the mortality rate was 40% among those who developed an HAI *vs.* 22.7% for colonization (OR 2.27). Similarly, for patients with CCI=2 the mortality rate was 47.1 *vs.* 18.4% for HAI and colonization, respectively (OR 3.94, $p = 0.009$), for patients with CCI=3 47.6 *vs.* 28.6% (OR 2.27), for pa-

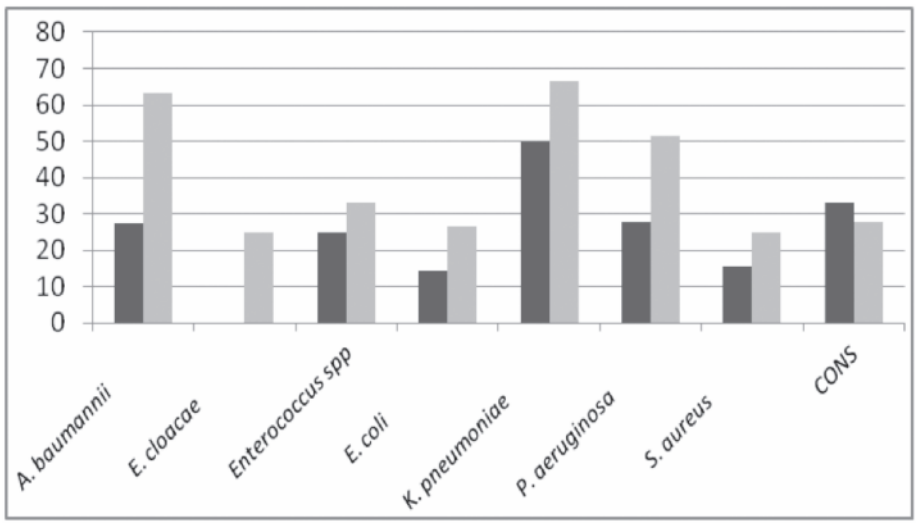

Figure 4. Mortality rate among patients whit one positive culture according to the bacterial isolate.
Light gray: HAI; dark gray: colonization

Table 3. Mortality rate and odds ratio (OR) among patients with one positive culture, in the different Units involved in the study.

Ward	HAI	Death		Rate	OR
		No	Yes		
Infectious disease	**No**	52	6	0.1	1.15
	Yes	10	1	0.09	
Nephrology	**No**	4	0	-	9
	Yes	1	1	0.5	
Medical oncology	**No**	10	0	-	10.92
	Yes	12	6	0.33	
ICU	**No**	44	19	0.3	2.25
	Yes	37	36	0.49	

tients with CCI=4 41.7 *vs.* 50% (OR 0.71), and for patients with CCI=5 26.3 *vs.* 13% (OR 2.38). The median length of hospital stay was 16 days for patients who developed a HAI *vs.* 9 days for those with colonization (Figure 5).

Group 2: patients with two or more bacterial isolations

In group 2, 92.3% of patients were admitted to ICU and 97.7% had an implanted device. 33.5% of subjects developed an HAI, 38.1% experienced 2 HAIs and 12.2% more than 2 HAIs. The mortality rate among patients with simple contamination was 23.8%, 31.8% for those who developed an HAI, 44% for those who developed 2 HAIs and 56.3% for those who developed 3 or more HAIs.

The median number of days of hospitalization was 15 days for patients with only contamination, 28 days for patients with an HAI, 34 days for those with 2 HAIs and 37 for those with 3 or more HAIs.

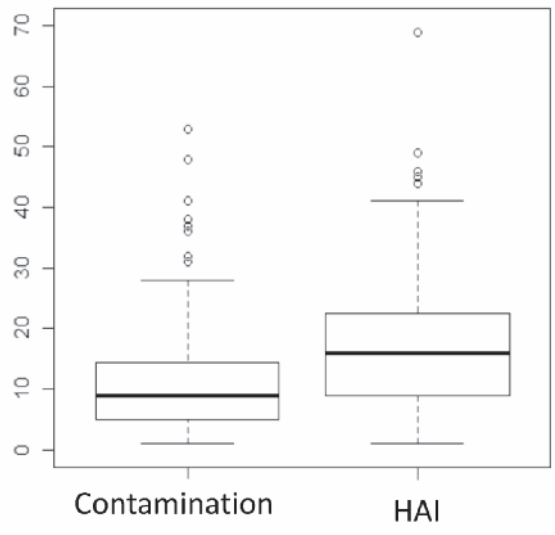

Figure 5. Median length of hospital stay (days) for patients with a single positive culture divided in two groups, according to the presence of HAI or colonization.

DISCUSSION

HAIs are a major public health issue, in terms of morbidity, mortality and costs. In the present study, as expected, the highest number of HAIs occurred in the ICU. In the ICU we observed the majority of patients who developed more than one HAI. This is very likely connected with the highest percentage of simultaneous use of invasive devices.

Respiratory infections were higher in the ICU. This is certainly related to the use of mechanical ventilation. BSI were prevalent in Infectious Diseases, Medical Oncology and Nephrology. However, the infection rate for the number of positive cultures is greater in Medical Oncology, followed by ICU, Nephrology and Infectious Diseases. This phenomenon may be due to the increased presence of immunosuppressed patients, the number of underlying diseases and comorbidities or therapies practiced in the oncology ward.

The mortality rate increases with age, CCI score and number of HAIs. Several authors have reported an increased ICU mortality in patients who acquired nosocomial infections[4-6]; a recent study showed a significantly higher mortality rate for HAI if compared to the community acquired infection (CAIs)[7]. Poor outcomes among patients with HAI were linked to the higher rates of polymicrobial/multiple sites of infection, higher APACHE II scores, ARDS and comorbidities[4,6,8]. However, factors that may have an impact on the outcome can fluctuate over time: aging population was found to be strongly associated with mortality in some studies[6,9,10] and higher rate of multi-resistant microorganisms may be an explanation for this change over time[11].

The number of HAIs occurring during hospitalization also correlates with the median length of stay. Length of stay was longer among patients in ICU, patients aged between 50 to 60 and among those with CCI score equal to 1.

Important differences were observed among patients with a single positive culture and on the basis of the etiological agent. Highest infection rates were recorded in patients with positive cultures for *A. baumannii* and *P. aeruginosa*. The development of an HAI by *A. baumannii* was an important risk factor for death during hospitalization. However, consistently higher mortality rates were observed among patients with HAI, compared to those with just contamination, for each etiologic agents included in the study. Of particular importance are the results of patients with positive culture for *E. cloacae*: in these cases death occurred only among patients who developed an HAI.

Among patients who developed an HAI, higher mortality rates were observed for those who have developed a CLABSI or VAP. Although affected by the small sample size, it is important to highlight that all the HAIs with lower prevalence (BRON, IAB and RH) had a very high cumulative mortality, probably because they are less common and more difficult to manage in terms of diagnosis and therapy.

In keeping with previous studies[12], we also found that infections were more common among patients older than 50 years, decreasing significantly in younger patients.

The highest infection rates were observed among patients hospitalized in Oncology and ICU. All patients who died in Oncology and Nephrology, with only one positive culture, had developed an HAI during the hospitalization. The risk of death is double in ICU, but it seems irrelevant in Infectious Diseases. This seems to be linked to the rates of resistance of the isolated bacteria in each ward and to the severity of underlying disease according to the CCI.

Males appear more frequently infected than females. However, when females acquire an HAI, they have an increased risk of death during hospitalization. Sex could be considered as an additional risk factor.

The risk of infection was greater for patients with invasive devices. This is related to the comorbidity between patients carrying device and the greater possibility of entry of microorganisms in these patients. The risk of death for patients with device was more than three times than that of patients without device. However, although a relationship between the presence of an invasive device and the emergence of a HAI exists, the link with mortality is spurious.

Of importance, the probability of infection increases with increased length of stay. In fact, patients who develop a HAI have a longer hospital stay compared to those with only contamination. HAI directly correlated with the length of hospital stay in other study where the average length of stay was 20.6 days for cases with HAIs in comparison to 4.5 days in cases without one[13]. Hence, underlying clinical conditions become very important. Numerous studies showed the importance of gastrointestinal disorders to generate infections, because of immune-microbiological characteristics of the intestine[14]. Moreover, it was found that microbial translocation may be accompanied by the diffusion of infective agents into the systemic blood stream[15]. In addiction, alteration in motility, mucosal defenses and microflora allow enteric bacteria translocation into mesenteric lymph nodes and then to the bloodstream[16].

In the group of patients with two or more positive culture tests the mortality rate and, consequently, the length of stay progressively increased with the number of HAIs. In a study published in 2006, it was proved that standard surveillance methods based on frequent data analysis and feedback, interventions based on guidelines and protocols applications allow to achieve reductions in HAI rates. Moreover, decreasing HAIs considerably diminished the economic weight of infection: it was calculated that the decline in BSI and VAP alone yielded savings of $578,307 to $2,195,954 per year at the study hospitals[17].

The present study highlights the need for strict epidemiologic control of microbial resistance, infections surveillance in all wards, as well as the improvement and maintenance of safe and sterile conditions and procedures by the hospital personnel.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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