

Central vascular catheter infections in a Hospital of Central Italy

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SUMMARY

The insertion and the permanence of central venous catheters (CVC) represent potential sources of infection contracted in hospital. The evaluation of the risk of CVC-associated infections was evaluated in a retrospective study during the period 2007-2010 in a Hospital of Central Italy. A total of 514 CVC were collected and examined by microbiological techniques and, among the examined patients, 450 CVC blood cultures were collected. Cultures were performed collecting a portion of 5-6 cm of intravenous catheters in liquid medium and spread on selective media for Gram-positive and Gram-negative bacteria and yeasts; blood specimens were obtained through peripheral venous punctures and analyzed by a commercial automated system. 308/514 (59.90%) samples were positive to the microbiological culture. *Staphylococcus aureus*, *S. epidermidis* and other coagulase negative Staphylococci (CNS) were the prevalent Gram-positive bacteria. Among Gram-negative bacteria, Enterobacteriaceae and Pseudomonaceae were the main bacteria isolated. A higher prevalence of Gram-positive bacteria was observed in Neonatal Pathology (90.90%). The Intensive Care Unit (ICU) showed 73.10% of positive cultures with 54.12% of Gram-positive isolates. Among positive blood cultures (38%), Gram-positive bacteria were the main bacteria isolated. The high prevalence of catheter-related infections requires accurate surveillance and the assumption of preventive measures in particular during catheter insertion.

KEY WORDS: Central venous catheter, Gram-positive and Gram-negative bacteria, Blood cultures, Hospital infections.

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INTRODUCTION

Infections contracted in hospital are caused by a diverse set of factors and vascular accesses, in particular, the insertion and the permanence of central venous catheters (CVC) represent potential sources of infection. In these cases, the risk of infection is related to the procedures for catheter administration, therefore a correct procedure of insertion can significantly reduce

these complications (Delgado-Capel *et al.*, 2012; O'Grady *et al.*, 2011).

CVCs have particular relevance among the various implantable devices for their widespread use in diagnosis and therapy. Vascular catheters, by definition, are devices capable of realizing a feedback process between the human body and the external environment, and are used for various purposes from the monitoring of vital signs to the administration of nutrients and pharmacologically active substances (Castagnola *et al.*, 1996).

In general, more than half of the patients in a hospital are routinely subjected to infusion therapy for the administration of drugs, blood products, intravenous liquids or hemodynamic monitoring. These devices are made of different polymeric materials, with high biocompat-

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ibility and characterized by mechanical, morphological and chemical-physical properties that allow easy trans-cutaneous insertion with little trauma (Baldassarri *et al.*, 1994; Lutolf *et al.*, 2005).

A biocompatible material should not release components (solvents, catalysts or degradation products) that may be directly or indirectly toxic into the environment of the body in which it is implanted (San Juan *et al.*, 2009). The major complication associated with use of implantable medical devices, and in particular CVC, is represented by the onset, even a very short time from their insertion, of infections associated with these devices, with the consequent failure of the implant and the need of their removal (Lavery, 2010; National Collaborating Centre for Nursing and Supportive Care, 2003).

This risk is very high, not only in patients with immune deficiencies, but also in immunehalthy subjects, in whom the mere presence of the artificial device causes a lowering of the natural defenses, with a consequent increased risk of developing phlebitis, septicemia and, in some cases, bacterial endocarditis (Deshpande *et al.*, 2005; Lee *et al.*, 2006; Terpenning *et al.*, 1988).

The insertion of a catheter may seriously compromise the patient defense mechanisms towards the infection, represented by the natural anatomical barriers and by the immune system; in fact, crossing the skin barrier provides a direct route of invasion for bacteria and yeasts. The insertion of the catheter may also, directly or indirectly, decrease the local defences of the patient; *in vivo* studies have shown that phagocytosis and bactericidal activity of the cells of the immune system decrease in the presence of devices made of poly-tetra-fluoroethylene and poly-methyl-methacrylate materials (Kaplan *et al.*, 1999).

The greater or lesser frequency of isolation of the different pathogens depends both on the type of device used and on the area of the body concerned (Collins, 2008). The largest number of infections is caused by *Staphylococcus aureus*, *S. epidermidis* and other coagulase negative Staphylococci (CNS). Yeast infections, in particular *Candida* spp., occur only in a small percentage of cases, while the remaining infections are caused by other Gram-positive (*Enterococ-*

cus faecalis, *E. faecium*, etc.) and by Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, etc.) (Kojic and Darouiche, 2004; Nicoletti *et al.*, 2006; Shenep *et al.*, 2011).

The purpose of this study was to evaluate the infectious risk associated with the placement and permanence of CVC through a retrospective study on cultures and CVC-blood cultures during the years 2007-2010 in the 'A. Cardarelli' Hospital in Campobasso, Central Italy.

MATERIALS AND METHODS

This retrospective analysis was conducted by reviewing records of cultures and CVC blood cultures performed in the 'A. Cardarelli' Hospital in Campobasso (Central Italy) in six different wards: Surgery, Nephrology and Dialysis, Infectious Diseases, Oncology, Neonatal Pathology and the Intensive Care Unit (ICU) from 2007 to 2010.

Surgical and immunocompromised patients, patients with chronic renal failure undergoing hemodialysis and patients with cancer were included in this study. When patients had a temperature of 38°C or higher, blood cultures were also collected.

Sample collection

A total of 514 samples were collected for CVC cultures. From the patients, after cleaning the skin catheter junction with alcohol, the CVC was removed with sterile forceps.

Using sterile scissors, a portion of the intravenous catheter (5-6 cm), was cut, immersed in sterile Nutrient Broth (NB, Oxoid, Milan, Italy) and immediately sent to the laboratory for the bacterial culture.

Culture conditions and bacterial identification

The samples inoculated in NB (Oxoid) were incubated in aerobic condition at 37°C for 24 h. Subsequently, aliquots of 100 µl were spread onto selective media: Mannitol salt agar (Oxoid) for the detection of *Staphylococcus* spp.; Enterococcosel and Deoxycholate agar (Oxoid) for the differential isolation and presumptive identification of *Enterococcus* spp.; Cetrimide agar (Oxoid) for the detection of isolation of *P.*

aeruginosa and Sabouraud agar (Oxoid) for the isolation of yeasts. All plates were incubated in aerobic condition at 37°C for 24 h, except for the Sabouraud agar plates which were incubated in aerobic condition at 25-28°C for five days. Cultures were considered positive when $\geq 10^2$ c.f.u./ml were detected (Sadoyma *et al.*, 2006). Microbial identification was performed by the commercial automated system BD Phoenix (Becton Dickinson Italia S.p.A., Buccinasco, Milano, Italy). Microbial identification was based on a total of 45-46 biochemical colorimetric and fluorimetric reactions, and allowed the distinction of a large number of microorganisms (more than 140 species of Gram-positive and more than 160 species of Gram-negative).

Blood cultures

Among the 514 examined patients, 450 blood cultures were performed. Blood specimens were obtained through peripheral venous puncture. Blood cultures were analyzed using the Automated BD Bactec 9120 (Becton Dickinson S.p.A. Italy), which provides for the collection of the sample from the patient's bedside with BD BACTEC bottles.

The BD BACTEC 9120/F is a fluorescent system that allows completely automated reading of blood samples and samples of other normally sterile body fluids for bacteriological research. With a remarkably shorter testing time and higher sensitivity than traditional methods, the system detects aerobic and anaerobic microorganisms, yeasts and mycobacteria. The BD BACTEC bottles contain broth formulations suitable for a specific quantity and type of research (bottles and land for aerobes, anaerobes, yeasts, mycobacteria) with an injection volume of 3-10 ml bottles for non-pediatric and 0.1-3 ml bottles for children. After seven days, positive samples were sub-cultured and susceptibility tests were performed with the BD Phoenix automated system. The evaluation of procalcitonin levels that represent a good indicator of bacteremia was used to avoid false positive samples (Kasem *et al.*, 2012).

Data analysis

Data analysis was performed using the statistical program SPSS (Statistical Package for Social Science: SPSS for Windows Version 13.0,

SPSS Inc., Chicago, IL, USA, 2004). χ^2 -test was the statistical test used for comparison of data.

RESULTS

This retrospective study evaluated the infection risks related to the presence of CVC in in-patients between 2007 and 2010.

Prevalence of CVC infection for ward

In the examined period, 514 samples were collected, and 308 were positive, corresponding to 59.90% of the total catheterizations. Analyzing the 308 positive cultures, and taking into consideration the wards with a significant percentage of demand for cultures, we obtained percentages of infections as shown in Figure 1.

In particular, in the ward of Oncology high percentages of infections were recorded (with peaks of 100%) and in ICU a substantial increase over the four years of observation was detected ($P < 0.01$).

High prevalence was also evident in the Nephrology and Dialysis ward, with consistent high values between 69.20% in 2007 and 78.90% in 2009. In contrast, the Surgery ward, after a steadily increasing trend through 2007-2009, displayed a decrease of positive samples in 2010 (45%). Opposite was the trend in the Infectious Diseases ward, after a continuous decrease of infection in the 2007-2009 period, an increase in 2010 (78.60%) was shown. Finally, in Neonatal Pathology, despite a reduction in the last year of observation, a substantially constant trend was recorded.

Microbial species most responsible for CVC infections

The microbial species most frequently responsible for CVC-related infection belonged to the Gram-positive cocci, in which Staphylococci (*S. aureus*, *S. epidermidis*, CNS) appeared frequently, and the prevalence of these remained unchanged over the years (75%) with respect to the Gram-negative bacteria. The isolation of yeasts was not significant in each ward during the time of study (data not shown).

Figure 2A shows the prevalence of infections caused by Gram-positive cocci from CVC occurring in the years under review, showing that

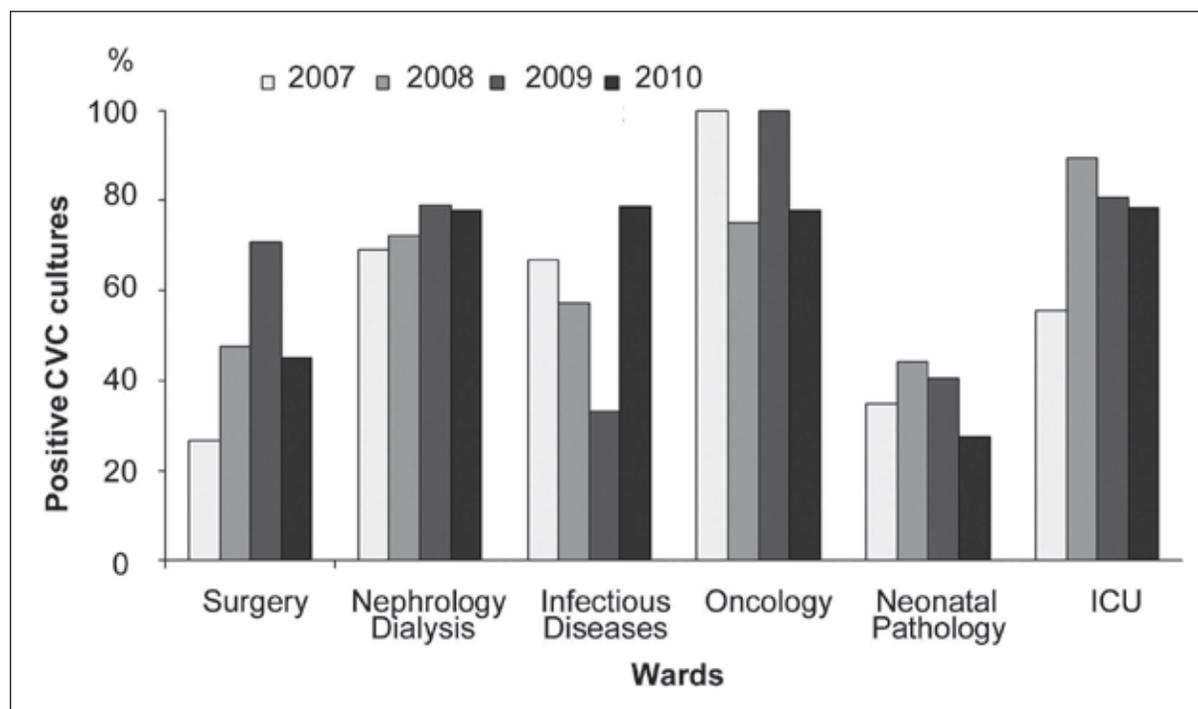


FIGURE 1 - Positive CVC cultures in the analyzed hospital wards in time.

most infections were caused by CNS (43.08% in 2007, 31.25% in 2008, 49.48% in 2009 and 38.46% in 2010) in a high average trend.

Staphylococcus epidermidis (Figure 2A) was responsible for only 10.80% of infections in 2007, 16.71% in 2008, 9.30% in 2009 and 14.31% in 2010. *Staphylococcus aureus* was responsible for 13.90%, 12.50%, the 10.30% and 5.51% of CVC infections in 2007, 2008, 2009 and 2010, respectively. Enterococci (group D Streptococci) were present in CVC infections in an amount of 4.60% in 2007, 13.50% in 2008, and 4.10% and 8.81% in 2009 and 2010 ($P < 0.05$), respectively.

The Gram-negative bacteria, belonging to the family Enterobacteriaceae and Pseudomonaceae, caused infections in only 25% of total cases. To facilitate data analysis, the isolated species were grouped together and considered in the corresponding genus. Figure 2B shows the different species of Gram-negative bacteria whose focal point was the prevalence of infections due to *Enterobacter* spp. in 2007 (13.80%) and a sharp drop in the percentage in 2008 (2.10%) and 5.10% and 10% in 2009 and 2010 ($P < 0.05$), respectively. Percentages of 6.11% and 7.31% in

2007 and 2008, respectively, followed by a reduction in percentage to 1% and 2.21% in 2009 and 2010, respectively, were found for *Pseudomonas* spp. (especially *P. aeruginosa*). Together with *Pseudomonas* spp., the presence of the genus *Acinetobacter* was significant (especially the species *A. baumannii* and *A. calcoaceticus* complex), responsible for opportunistic infections in individuals with immune deficiencies, and inherently resistant to the main antibiotic molecules.

Analysis by ward

Neonatal Intensive Therapy and the ICU were the wards in which more CVCs were used, because in-patients were found to be permanent carriers of CVC, both to receive parenteral nutrition and drug therapies to meet the needs of analytical biochemistry and microbiology.

In the Neonatal Pathology ward (Figure 3A), 146 CVC cultures were performed, of which 53 tested positive, amounting to 36.30%, which is the closest to the hospital average. The data analysis performed on the presence of 44 species of microorganisms showed a fall in the prevalence of infections caused by Gram-nega-

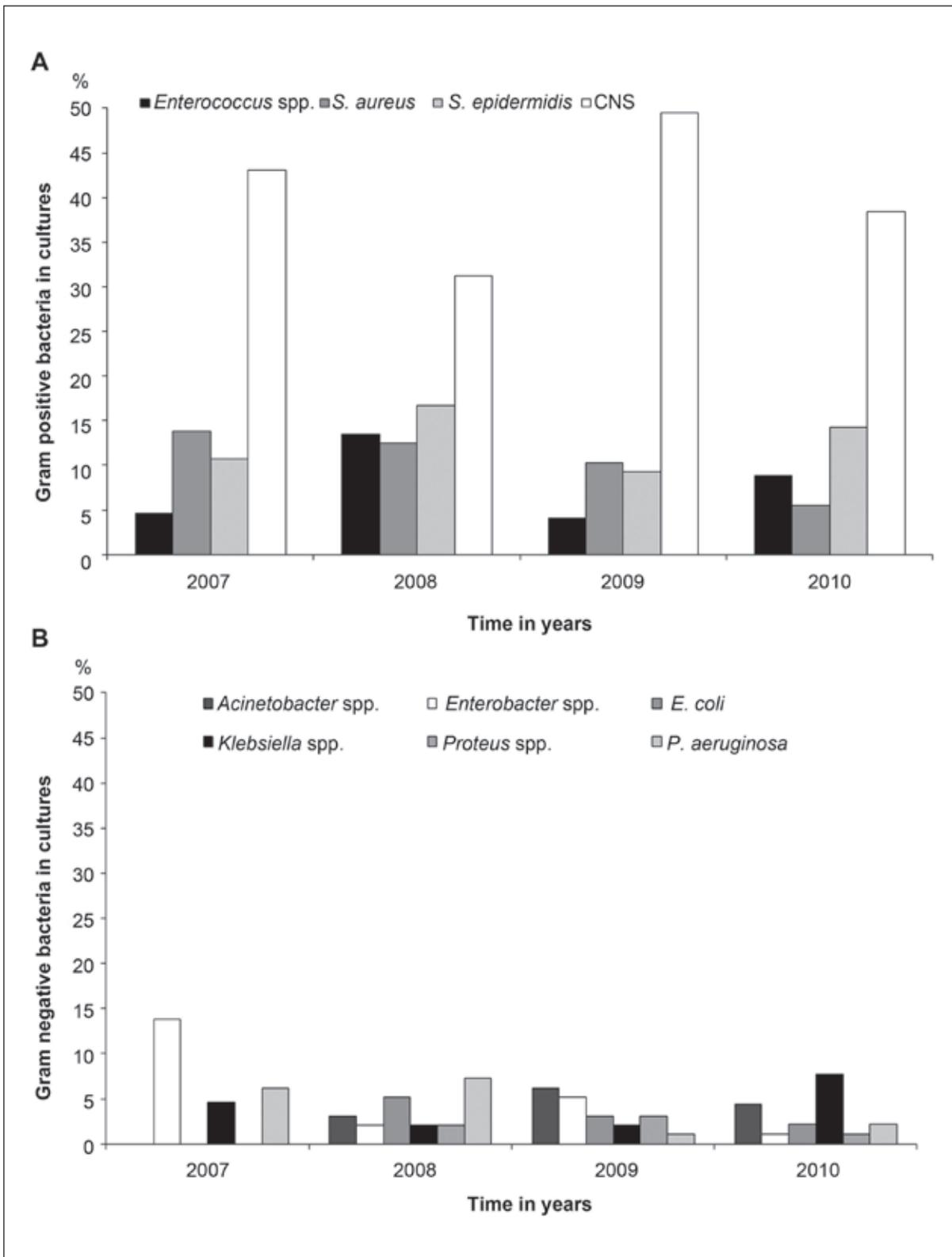


FIGURE 2 - Gram-positive (A) and Gram-negative (B) bacteria in CVC infection over time.

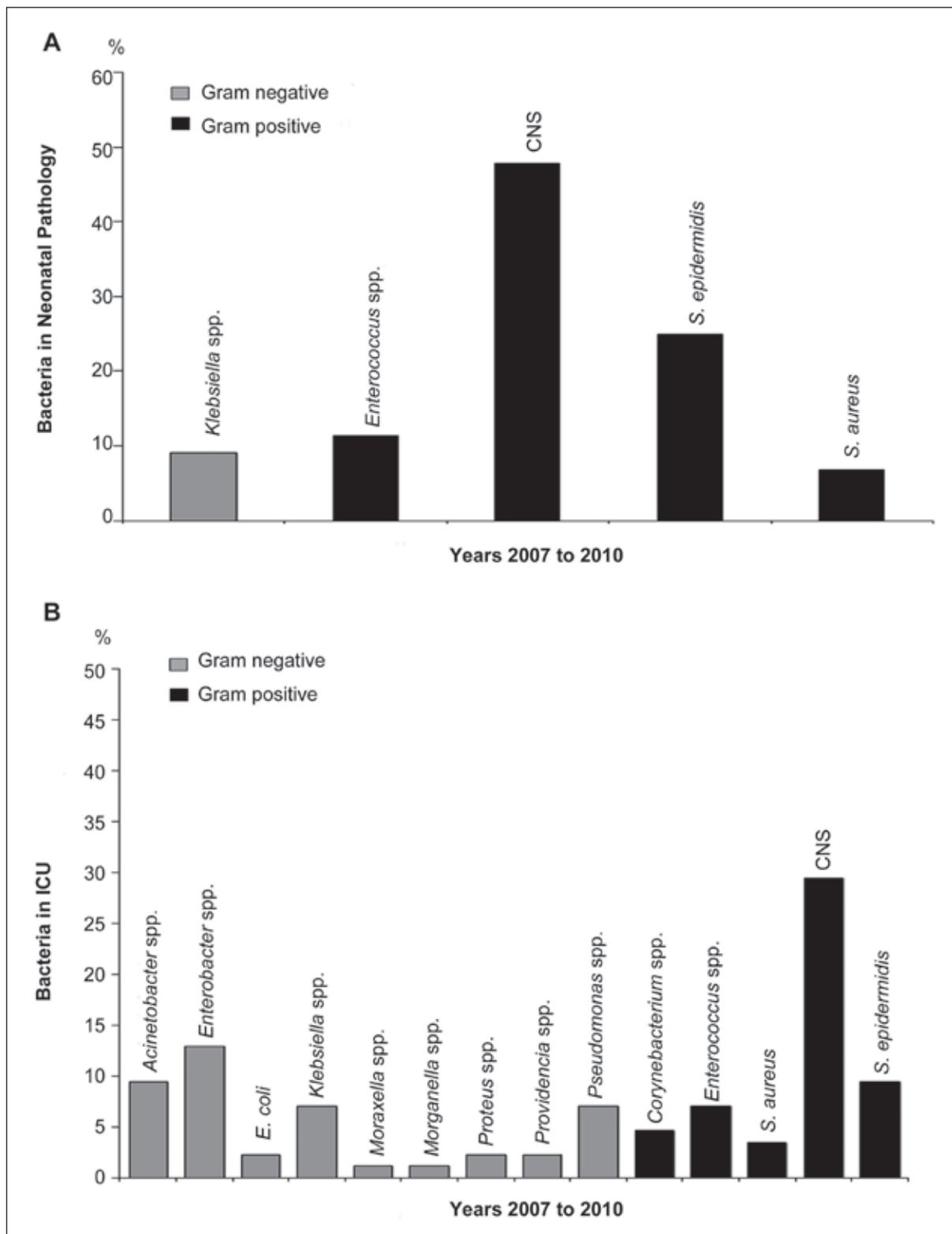


FIGURE 3 - Gram-positive and Gram-negative bacteria in the ICU over time (A); Gram-positive and Gram-negative bacteria in Neonatal Pathology over time (B).

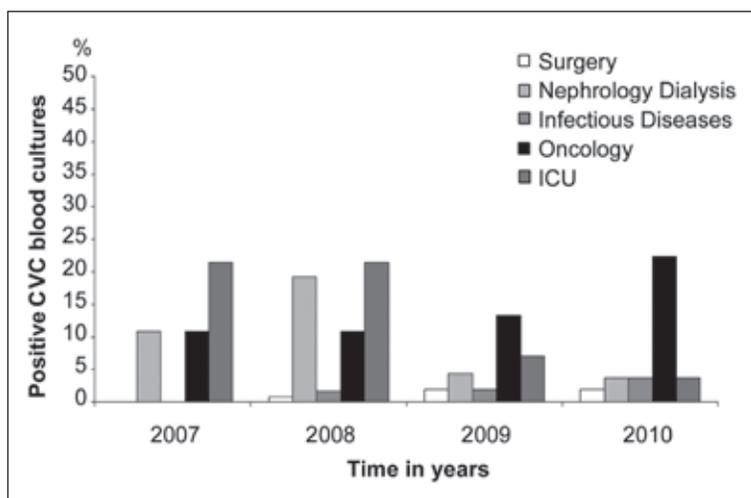


FIGURE 4 - Positive CVC blood cultures in the hospital wards analyzed over time.

tive bacteria (9.10%); in fact, 91% of CVC infections were supported by Gram-positive cocci. Among the Gram-negative bacteria only the presence of *Klebsiella* spp. was reported (9.1%) while among the Gram-positive bacteria, Staphylococci (CNS 47.8%, *S. epidermidis* 25%, *S. aureus* 6.8%) and *Enterococcus* spp. were detected (11.4%) (Figure 3A).

Between 2007 and 2010, 104 catheter cultures were performed in the ICU, 76 of which were positive, equal to 73.11%, a significant difference from the overall positivity rate of 59.90%. In the ICU ward, 85 microorganisms were identified from cultures of CVC, of which 54.10% were Gram-positive and 45.90% were Gram-

negative. Data analysis showed an increase in infections caused by Gram-negative bacteria, especially *Enterobacter* spp., *Pseudomonas* spp., *Klebsiella* spp. and *Acinetobacter* spp., 45.90% compared to the 25% global hospital average (Figure 3B).

Among Gram-positive bacteria, CNS were the microorganisms mainly isolated (29.40%) followed by *S. epidermidis* (9.40%) and *Enterococcus* spp. (7.10%).

Blood cultures from CVC

During the four years of study, there has been a significant increase in requests for blood cultures from CVC (65 in 2007, 120 in 2008, 158 in

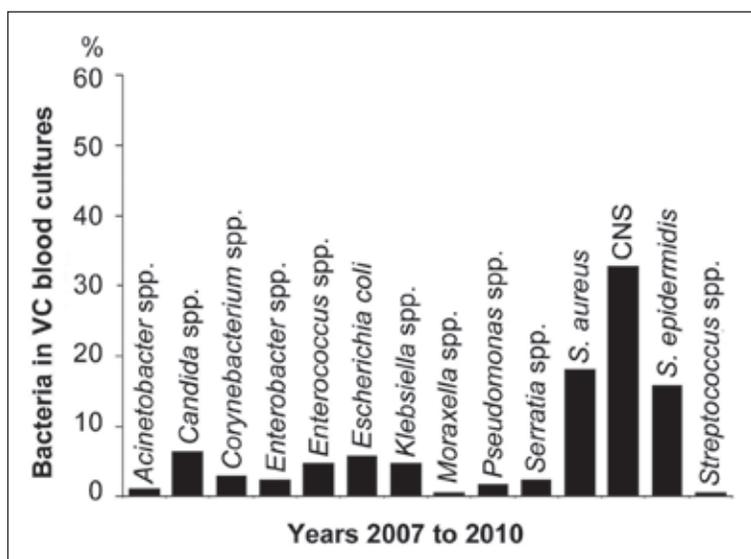


FIGURE 5 - Gram-positive and Gram-negative bacteria in CVC blood cultures over time.

2009 and 107 in 2010). Figure 4 shows the percentage of positive cases for ward of CVC blood cultures. All these positive results coming from patients with high levels of procalcitonin. In the wards of Nephrology/Dialysis and ICU, a sharp decline in percentages of positive cases has been found. In particular, in ICU ward the positive cases in time decreased from 20% to 4% ($P < 0.01$). The ward of Oncology deserves a special mention, since its trend showed a tendency to increase in positive cases (from 10.80% in 2007 to 22.40% in 2010).

Figure 5 shows the prevalence of microorganisms that cause positive blood cultures from CVC. It is important to note that the majority was due to Gram-positive cocci (CNS 32.70%, *S. aureus* 18.11% and 15.80% *S. epidermidis*).

DISCUSSION

Our retrospective study shows that there is a growing demand for CVC examinations, also due to an increase in the use of this medical device in clinical practice. In the four years studied, the data show a fairly high percentage of positivity.

The Surgery, Nephrology and Dialysis, ICU, Oncology and Neonatal Pathology wards were characterized by many positive cultures. These detected data emphasizes the need of improve the preventive measures to decrease the rate of CVCs infection. As reported by Walshe *et al.* (2012), thought a study conducted in 12 years, a continued vigilance can be useful to reduce significantly the CVCs infection rate. The microbial species most frequently responsible for catheter-related infections generally belonged to the population of Gram-positive cocci whose prevalence remained unchanged over the four years of examination. In particular, among Gram-positive bacteria, CNS were the most common isolates demonstrating the primary role played by these opportunistic microorganisms in catheter infections (Guidet *et al.*, 1994). Therefore, the reasons why the majority of CVC infections were related to these bacteria are clear; in fact, for the insertion of the device, an incision is first made on the skin to create a venous access and then the CVC is inserted intravenously (Moro *et al.*, 1994; O'Grady *et al.*,

2002). The passage through the skin, as well as the manipulation by the medical staff, causes the CVC bacterial contamination, even if the bacteria involved were simply part of the normal bacterial flora.

Of interest is the case of sepsis recorded by Mosele *et al.* (2012) due to *Corynebacterium macginleyi* that does not represent an ordinary pathogen, but, in conditions of immunodeficiency, can favor an opportunistic infection. The pathogenic behavior of nosocomial causative microorganisms was strictly related to the health of the subject: patients with immune deficiencies, regardless of cause, were particularly susceptible to attacks by bacteria. The success of the management of the infectious is also complicated by the remarkable bacterial resistance to chemo-antibiotics (Khayr *et al.*, 2012; Raad and Hanna, 2002). The antimicrobial resistance among bacteria isolated in nosocomial patients represents a crucial problem that requires an efficient surveillance system in the wards. In particular, the resistant microorganisms beta-lactamase-producing, methicillin-resistant and mupirocin-resistant at high levels, have assumed considerable importance in the acquisition of resistance to chemo-antibiotics (National Collaborating Centre for Nursing and Supportive Care, 2003; Naves, *et al.*, 2012; Nicoletti *et al.*, 2006; Raymond and Aujard, 2000). Moreover, CNS were especially able to colonize the CVC because of their ability to produce matrix, through which they adhere firmly to the materials of which CVCs are made, forming a biofilm which makes it difficult for the immune system or the antibiotics to attack (Newman *et al.*, 2012; Sander *et al.*, 2012).

A significant reduction of Gram-negative bacteria was observed in Neonatal Pathology. Interestingly, *Klebsiella* spp. were the only Gram-negative bacteria detected suggesting the need to monitor this sepsis to improve care quality. These data were also found by Couto *et al.* (2007), who isolated *Klebsiella* spp. during a ten-year prospective surveillance of nosocomial infections in neonatal intensive care units, as the most frequent agents among Gram-negative bacteria in developed countries. An increase in infections caused by Gram-negative bacteria, especially *Enterobacter* spp., *Pseudomonas* spp. and *Acinetobacter* spp. was detected in the ICU,

where the presence of this bacteria is endemic (Guidet *et al.*, 1994; Moro *et al.*, 1994). In fact, they were routinely detected in all biological materials processed (bronchial aspirate, urine culture, blood culture). CVC infection is often associated with the risk of systemic infection (sepsis), especially in immune deficient patients, detected by blood culture from CVC. The results obtained for CVC blood cultures displayed general low levels of infection similarly consistent with those reported previously to other authors (Darby *et al.*, 1997; Walshe *et al.*, 2012).

Interestingly, in ICU wards a significant reduction of infection was detected and this can be attributed to a general increase in infection control awareness.

The high prevalence of CVC infections requires the adoption of preventive measures to limit contamination of the catheters themselves. Surely, it is essential that hospital staff involved in case of patients with CVC is trained about infection prevention practices.

Antisepsis of the skin, daily inspection of the insertion site, disinfection of the external pathway of access and removal of the catheter in case of positive culture can contribute to the control of these widespread hospital infections.

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