

ANTIMICROBIAL RESISTANCE PROFILE IN INFECTIOUS DISEASE HOSPITAL INTENSIVE CARE UNIT

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Abstract

The aim of the study was to assess the profile of nosocomial infections and antibiotic resistance in the Intensive Care Unit (ICU) department *versus* other departments of the „Dr Victor Babeș” Infectious Diseases Hospital, Bucharest, Romania. The descriptive and documentary study in transversal approach based on analysis information provided by the national and international data bases was completed with the active surveillance results of the Microbiology Laboratory. There was described and identified the profile of nosocomial infections and antibiotic resistance in the intensive care unit (ICU) department in comparison to the global resistance of other departments of the hospital, during December 2011- May 2012. Microorganisms included in the assesment were: *Staphylococcus aureus* MRSA, *Enterobacteriaceae* (*E. coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*), *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. For all these microorganisms the resistance was higher in the ICU than the antibioresistance in other compartments of the hospital, fact that highlights this particular department as a critic point in the control of nosocomial infections.

Rezumat

Scopul studiului a fost acela de a evalua profilul etiologic al infecțiilor nosocomiale și rezistența la antibiotice în Secția de Anestezie și Terapie Intensivă (ATI) în raport cu rezistența globală în celelalte secții ale Spitalului Clinic de Boli Infecțioase și Tropicale „Dr Victor Babeș”- București, în vederea identificării direcțiilor de intervenție viitoare. Studiul descriptiv și documentar în abordare transversală a fost realizat pe baza informațiilor furnizate de analiza datelor naționale și internaționale, completate cu rezultatele supravegherii active derulate de Laboratorul de Microbiologie al Spitalului. A fost analizată comparativ rezistența la antibiotice în ATI și antibioresistența globală în celelalte secții ale spitalului, în perioada decembrie 2011 - mai 2012. Microorganismele țintă pentru această analiză au fost: *Staphylococcus aureus* MRSA, *Enterobacteriaceae* (*E. coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*), *Pseudomonas aeruginosa* și *Acinetobacter baumannii*. Rezultatele testelor de laborator au evidențiat faptul că pentru toate aceste microorganisme rezistența a fost mai mare în Secția de ATI decât cea de la nivelul celorlalte secții ale spitalului. Concluziile studiului identifică secția de ATI ca un punct critic în controlul infecțiilor nosocomiale.

Keywords: nosocomial infections, antimicrobial resistance, Intensive Care Unit (ICU).

Introduction

Nosocomial infections due to their consequences on morbidity, costs, safety and mortality still represent a public health issue all over the world [1, 4]. In this context, in the European Union (EU), according to the White Paper on Patient Safety from 2007, the measures aiming to reduce the burden of nosocomial infections are a priority. That requires national efforts for improving the surveillance systems, laboratory capacities, personal and population improvement of knowledge and practices. Antibiotherapy guidelines, training for professionals, comparable and standardized data collection methodology were elaborated and are currently implemented at EU level in Antimicrobial resistance interactive database (EARS-Net) and other specific partnerships [3, 6]. In this context the national adopted legislation, the Order of the Minister of Health no. 916/2006 regarding the approval of the surveillance, prevention and control of nosocomial infections in hospitals complemented with the yearly provisions of the ministerial orders regulating public health programmes, dedicating special resources and indicators represent an important frame in the national efforts to mitigate nosocomial infections and to prevent the antibiotic resistance [7]. In this context the roles of Laboratory of Microbiology (LM) are clearly established: management of control measures by the microbiologist contribution in the Board of control of nosocomial infection and ensuring the bacteriological diagnostic accuracy, the isolation, the correct identification of the etiologic agent, the determination of antibiotic resistance phenotype, in conditions of the quality management system, 15189:2007 Standard. Also, as supporting mechanism the Lab plays an important role both in passive, active and virtual surveillance [5, 9] in order to provide evidences for reduction of nosocomial infections, multidrug-resistance and their associate social and financial consequences [8, 10, 13, 23].

The aim of the present study was to assess nosocomial infections and antibiotic resistance profile in the ICU department in comparison to the other departments of the hospital.

Materials and Methods

A descriptive and documentary study was conducted in a transversal approach based on analysis of the information provided by the national and international data bases completed by the active surveillance results of the microbiology laboratory belonging to an infectious diseases clinical hospital aiming to describe and identify the profile of nosocomial infections and antibiotic resistance in the ICU department [19, 20]. We tested and analysed

antibiotic resistance of the bacterial strains isolated from the patients hospitalized in ICU department off during the period December 2011- May 2012.

We used in our clinical microbiology laboratory the Kirby Bauer Disc Diffusion Susceptibility Test of significant bacterial isolates. The most widely used testing methods include broth microdilution, E –test, or rapid automated instrument methods that use commercially marketed materials and devices.

We analysed comparatively the antibiotic resistance in this department and the global resistance in the other departments of the hospital, in the same time period. *Staphylococcus aureus* strains analysed were isolated from both nasal and rectal swabs (screening of colonization with multidrug resistant/ MDR bacteria) and in pathological samples taken from infected patients during hospitalization, from the different anatomical sites (upper airway, skin lesions, blood) [9, 10]. Microorganisms targeted for this analysis were: *Staphylococcus aureus* MRSA, *Enterobacteriaceae* (*E.coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*), *Pseudomonas aeruginosa* and *Acinetobacter baumannii* [11, 16]. The key antibiotics to which were performed testing and monitoring of treatment were selected as recommended by “M100-S24 Performance Standards for Antimicrobial Susceptibility Testing” / Clinical and Laboratory Standards Institute / CLSI 2011, 2012.

The study was carried out in the Infectious and Tropical Diseases Clinical Hospital “Dr. Victor Babeş” Bucharest, Microbiology laboratory based on prior approval of the hospital ethics committee.

Results and Discussion

Nosocomial infection level and associated effects: Nosocomial infection (NI) is internationally defined and recognized as one important public health issue. These infections are, from the patient perspective, one of the most unwanted events that might occur during the health services delivery, an event with, unfortunately, rather high probability, ranging between 1:20 to 1:10 in some countries. According the 2012 European Centre for Disease Prevention and Control (ECDC) data, based on pilot point prevalence survey carried out according to a standardised methodology in 66 hospitals from 23 countries, the EU prevalence in acute care facilities was 7.1%, completed of other approximately 4% in long term care facilities, counting for about of 4.1 million patients affected in acute care and another 2.6 million of cases occurred in long term care facilities [23]. And, of course their associated effects on pain, mortality (approximately 37,000 deaths

directly attributable only in Europe) length of hospitalization and individual associated costs [18, 21].

In addition, from the health care system and social point of view the direct annual costs generated by additional medical care of nosocomial infection, estimated only for Europe were 7 billion, according to the ECDC 2008 report [8, 21]. For example, data for Germany confirm the direct costs of about two million per year, while the indirect costs and those of post hospitalisation, including those related to revenue loss associated with them, which is estimated to be at least three times higher than direct costs [22].

Similarly, figures for United States reveals that a Health Care Associated Infection (HAI) practically doubles the hospital cost, with an attributable cost per case ranging from 9310 USD to 21103 USD together with an increase in length of stay (LOS) from 5.6 to 9.6 days [12, 17].

Intensive care unit nosocomial infections: Among the nosocomial infections, the Intensive Care Unit (ICU) infections are one of the most frequent nosocomial infections, counting for a risk of 20-30 of all ICU admissions, unfortunately predictable due to the extremely unfavourable ratio between patient vulnerability, numerous invasive medical procedures, specific medication affecting the natural resistance and frequently combined with an intempestive and non-selective unbalanced treatment and antibiotherapy, as synthetized by the EPIC study since 2000. The last evidences for nosocomial infections in ICU, according to the last EU intensive care units systematic surveillance, based on data reported by 14 countries, are confirming the role of ICU of epicentre, as considered in the speciality literature [2] counting for a prevalence of ICU acquired infections of: 5-9% for pneumonia, 3.1% for blood stream and another 3.2% for urinary tract infections, the main localisation for the starting point of antibiotic resistance [23, 24].

Resistance to antibiotics: Along with the nosocomial infection the burden of "multidrug" antimicrobial resistance, the newly acute emergent public health issue of the last years, has also specific features related to ICU epicentre. At a general level, according to the most recent information provided by the European Antimicrobial Surveillance Network (EARS-Net) [20] included in the ECDC 2012 Report, the main common issue of the antibiotic resistance (multidrug resistance), despite the large pathogen type, antimicrobial agent and geographical region variation, are: the methicillin-resistant *Staphylococcus aureus*, aminopenicillines, third generation cephalosporines and aminoglycosides *Klebsiella pneumoniae* and *E. coli* resistant; carbapenem resistance in *Pseudomonas aeruginosa*. According to the same Report, the ICU overall resistance pattern, (ECDC 2012) reveals

specific profiles for the isolated microorganisms, as following: 46% oxacilin resistance in for the *Staphylococcus aureus* MRSA isolates, 6% vancomycin resistance in *Enterococcus spp*, 22% ceftriaxone or cefotaxime resistance in *E. coli* isolates, 38% ceftriaxone or cefotaxime resistance in *Klebsiella spp* isolates and 52% ceftriaxone or cefotaxime resistance in *Enterobacter spp*.

Romanian situation and dynamics: The national data, seldom biased by the national legislation provision that generates a conflict between monitoring the quality and safety of care and the performance of the management, show a decreasing specific incidence for nosocomial infection among hospitalized patients from 223 to 179 incident cases in 100 000 patients discharged in 2011, comparing to 2007 figures [19]. Among those, the ICU infections, situated always on the first place as incidence, are maintaining the most negative dynamics, with the most spectacular increase from 2.17 in 2000 to almost 12/100000 discharged patients in 2011 [19]. Figures, obviously underreported, if we compare them to the results of the last prevalence study carried out in 2010 based on EDCC methodology in an acute care hospital, where the point prevalence of nosocomial infection was 6.6 %, with the hierarchy: wound sepsis, urinary tract infection, pneumonia [13, 14].

Comparative antimicrobial resistance of bacterial strains isolated in the ICU compartment and over all resistance in the hospital: Of the 100 patients investigated at admission and during hospitalization in the ICU department during the period December 2011 - May 2012, 61 developed respiratory tract infection, 36 patients were diagnosed with skin and soft tissue infections, 15 patients (majority carriers chronic urinary drainage) diagnosed with urinary tract infection and 3 patients were registered with acute and repeated diarrhoea syndrome with *Clostridium difficile*, *Staphylococcus aureus* strains analysed were isolated from both nasal and rectal swabs(screening of colonization with MDR bacteria) and in pathological samples taken from infected patients during hospitalization, from the different anatomical sites (upper airways, skin lesions, blood). MRSA strains were isolated at a rate of 69.5% in the ICU, compared with the percentage of 35.1% MRSA strains isolated in the hospital at the same time. Higher percentage of resistance was recorded also for ciprofloxacin: 52.2% in ICU, compared to only 8.3% in entire hospital. For macrolides, erythromycin is the key representative. Resistance of *Staphylococcus aureus* to erythromycin was of 76.3% in patients admitted to the ICU, compared to 45.4% resistant of the isolates strains in the entire hospital. There has been very small resistance (1.7%) registered to chloramphenicol and resistant 0.0% to vancomycin, linezolid and teicoplanin, both isolates in ICU and in

all other departments of the hospital. Of the total number of isolated *Staphylococcus aureus* strains, 69.5%, respectively 35.1% were methicillin-resistant/MRSA (resistance to all penicillins, cephalosporins I, II, III). Antibiotic resistance to all strains of *Staphylococcus aureus* is presented in order of decreasing percentage (Figure 1).

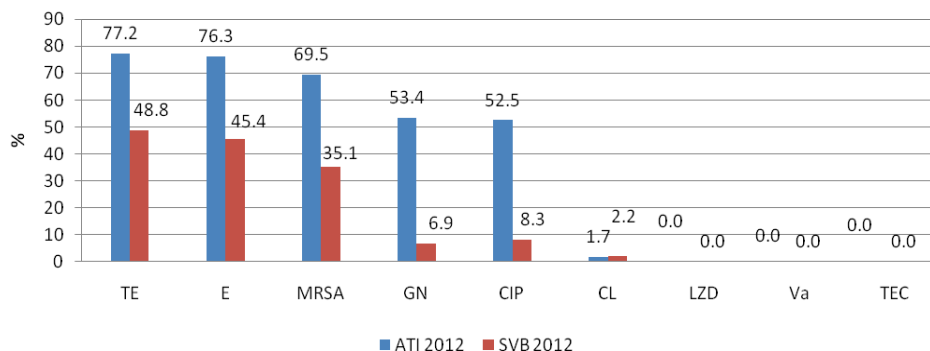


Figure 1

Antibiotic resistance of *Staphylococcus aureus* strains, compared in ICU, versus antibiotic resistance in other departments of the hospital (2012)

Note: TE=tetracycline, E=erythromycin, MRSA=meticilino-resistant *Staphylococcus aureus*, GN=gentamicin, CIP=ciprofloxacin, CL=chloramphenicol, LZD=linezolid, Va=vancomycin, TEC=teicoplanin.

Regarding *E. coli* in the ICU department, it had most of the resistance to ciprofloxacin (56.9%), 54.4% were strains producing extended-spectrum beta-lactamases (ESBL) and had no resistance to imipenem, as well as in the rest of the hospital. Resistance of *E. coli* strains isolated in the rest of the hospital was highest for trimethoprim-sulphamethoxazole (35.1%) (Figure 2).

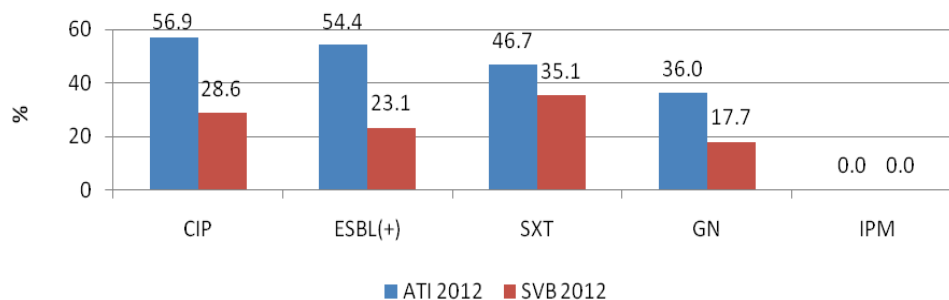


Figure 2

Antibiotic resistance of *Escherichia coli* strains, compared in ICU, versus antibiotic resistance in other departments of the hospital (2012)

Note: CIP=ciprofloxacin, ESBL(+)=extended-spectrum beta-lactamases, SXT=trimethoprim-sulphamethoxazole, GN=gentamicin, IPM=imipenem.

Klebsiella pneumoniae strains isolated in ICU compartment: 85.5% were producers of ESBL (resistance to all penicillins and cephalosporins generation I, II, III), 77.0% were resistant to ciprofloxacin, more than the strains isolated in the rest of the hospital (41.5% and 37.5%). It worth being mentioned that imipenem resistance was higher in strains of *Klebsiella pneumoniae* isolated in the hospital than in ICU compartment (7.1% and 1.6%, respectively) (Figure 3).

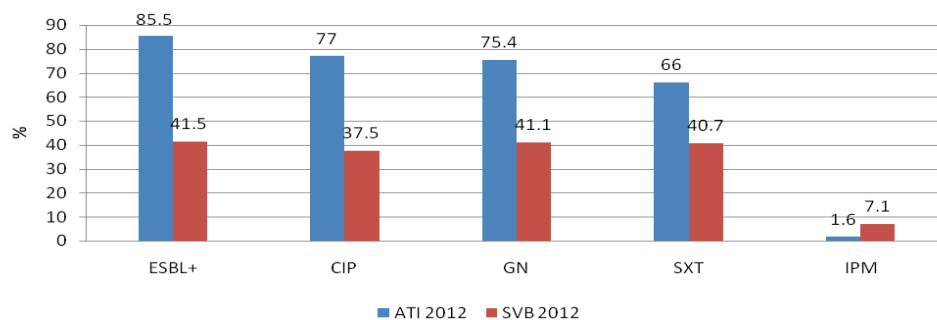


Figure 3

Antibiotic resistance of *Klebsiella pneumoniae* strains, compared in ICU, versus antibiotic resistance in other departments of the hospital (2012)

Note: ESBL(+)= extended-spectrum beta-lactamases, CIP=ciprofloxacin, GN=gentamicin, SXT=trimethoprim-sulphamethoxazole, IPM=imipenem.

Pseudomonas aeruginosa strains collected from the ICU department were resistant over 66% to all antibiotics tested except colistin, which were sensitive, while the resistance of the strains collected from hospital was between 19.5% to piperacilin-tazobactam and 28.0% to ciprofloxacin. They are also susceptible to colistin (Figure 4).

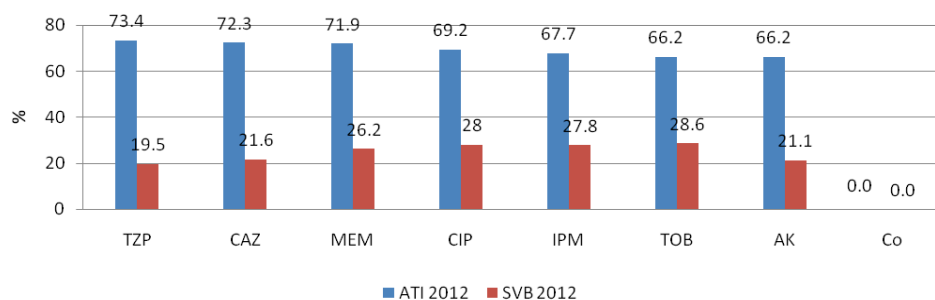


Figure 4

Antibiotic resistance of *Pseudomonas aeruginosa* strains, compared in ICU, versus antibiotic resistance in other departments of the hospital (2012)

Note: TZP=piperacilin-tazobactam, CAZ=ceftazidim, MEM=meropenem, CIP=ciprofloxacin, IMP=imipenem, TOB=tobramycine, AK=amikacine, Co=colistin.

Resistant strains of *Acinetobacter baumannii* collected from ICU was complete for piperacilin-tazobactam and over 90% for ceftazidim, ciprofloxacin, meropenem and imipenem but sensitive to colistin, while strains collected from the hospital had the highest resistance to ceftazidim (61.3 %), piperacillin- tazobactam (59.5%) and ciprofloxacin (57.7%), and were susceptible to colistin (Figure 5).

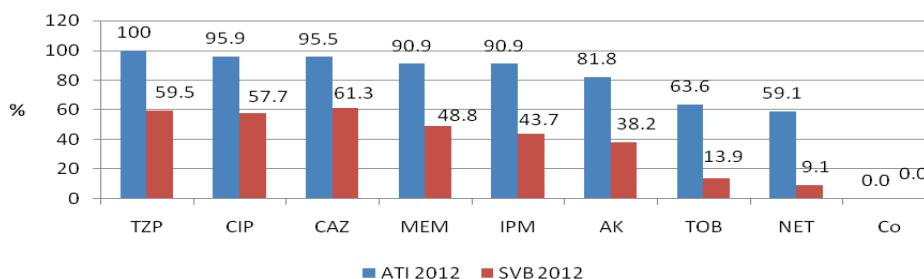


Figure 5

Antibiotic resistance of *Acinetobacter baumannii* strains, compared in ICU, versus antibiotic resistance in other departments of the hospital (2012)

Note: TZP=piperacilin-tazobactam, CAZ=ceftazidim, CIP=ciprofloxacin, MEM=meropenem, IPM=imipenem, AK=amikacine, TOB=tobramycine, NET=netilmicine, Co=colistin.

Interpretation of results: Porting of multidrug resistant organism (MDRO) is considered negative and precautions discontinued in the following situations: three negative screening tests (or 5 negative tests in ICU) performed at an interval of 1week, starting at least 48 hours of stopping antibiotic therapy or 2 negative screening tests for a patient who did not receive antibiotic treatment for several weeks.

Conclusions

ICU hospitalization is an important point determinant both to nosocomial infection and also to the general emerging antimicrobial resistance developed in the whole facility. It is important the screening of the patients, additional measures to comply with the conditions of hygiene, patient isolation and we should consider, also, the high percentage of multi drug resistance (MDR) in Romania (due to self-medication, treatment with broad spectrum antibiotics, the lack of uniform procedures and guidelines at the national level). That's why policies aiming to rationalize the antibiotic use in ICU are an important element in prevention. Strategies as de-escalation therapy, selective digestive decontamination, antibiotic rotation therapy and selective use of appropriate therapy, all included in clear and

restrictive rules and guidelines, in order to support implementation, should be pursued in all ICU.

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