



Original Contribution

CONSUMPTION OF ANTIMICROBIAL DRUGS AND ANTIBIOTIC RESISTANCE IN PROBLEMATIC FOR HOSPITAL INFECTIOUS PATHOLOGY BACTERIA

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ABSTRACT

Multiresistant bacteria are significant problem for the hospital infectious pathology and the antimicrobial resistance can result in increases morbidity, mortality and economic burden. The data in this study represent the consumption of antimicrobial drugs in a big hospital, expressed in a Defined Daily Dose (DDD) per 100 bed-days. The results, obtained in this respect show that 40.3 Defined Daily Doses per 100 BD were used during 2011 in the MMA hospital. There is 2.5 fold greater consumption of antimicrobials in our two ICU– 110.9 DDD/100 bed-days and 105.2 DDD/100 bed-days respectively and also in other high risky for infection development units, compared with the hospital as a whole. The antibiotics used most frequently at MMA were beta-lactam antibiotics with 59.5% or 24 DDD/100 bed-days, of which 13 DDD/100 bed-days are the quantities of the third and fourth generation of cephalosporins and 2.8 DDD/100 bed-days is a relative part of carbapenems. The use of quinolones was 6.1 DDD/100 bed-days and the quantities of aminoglycosides, spent in the hospital were 3.9 DDD/100 bed-days. All the data discussed in this study, suggest that nosocomial infections and antibiotic utilization need an improved infection control and monitoring to achieve definitive success in the infections treatment.

Key words: antibiotics, antimicrobial resistance, Defined Daily Dose per 100 bed-days

INTRODUCTION

Antibiotic resistance is an increasing problem worldwide. Dr. Margaret Chan, director general of the World Health Organization declared, that Antibiotic resistance could bring “ End of Modern Medicine as we know it ” /WHO Conference, March 16 2012, Copenhagen/ (1). The main cause of the rapid spread of bacteria, resistant to antimicrobials is the abuse and inappropriate use of antibiotics. Growing awareness of problems arising from over-use of antimicrobial agents has led to attempts to

develop policies or guidelines for rational treatment (2). In this sense, the determination of the Defined Daily Dose (DDD) is a very important issue, giving the information about the doses, used in various countries. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. (3). It should be emphasized that the DDD is a unit of measurement and does not necessarily correspond to the recommended or prescribed daily dose (PDD). The DDDs per 100 bed-days may be applied when drug use by inpatients is considered. The definition of a bed-day may differ between hospitals or countries, and bed-days should be adjusted for occupancy rate (3).

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The purpose of this study is to present data about antibiotic's utilization in a big Multiprofile hospital by the estimation of DDDs per 100 bed-days with regard to the possible assessment of the antibiotic resistance risk.

MATERIALS AND METHODS

Hospital

The study was carried out at Military Medical Academy /MMA/ in Sofia, Bulgaria for one year period of time – 01.01.2011 – 31.12.2011. Military Medical Academy is a community hospital with 800 beds. The hospital is a one of the national centres for trauma, respiratory disease, and liver transplantation patients' treatment. Antibiotic stewardship at Military Medical Academy /MMA/ includes all groups of antibiotics together with carbapenems, quinolones, third and fourth generations of cephalosporins. Because of that, that the MMA is a multiprofile hospital/ with eleven surgery units, two ICU – first is Anesthesiology and Resuscitation clinic (ARC) and second one - ICU for conservative therapy of patients from Dept of Internal Medicine/ it can be a pattern for the tendency in the bacterial resistance' development to antimicrobial drugs in Bulgaria, nevertheless the variety, detected in different regions in the world, countries, hospital to hospital in the same country, reported in this respect.

DDDs per 100 bed-days estimation

The total doses of antibiotics consumed were calculated and were technically quantified using an international measure-Defined Daily Doses per 100 Bed Days /DDD per 100 BD/. /Antibiotic Consumption Calculator – ABC.Calc v. 3.1/ (4)

RESULTS AND DISCUSSION

A total of 11681 samples, including urine, wound secrets, respiratory system samples, blood and puncta, sexual system samples and others, were investigated in the Laboratory of microbiology at MMA during 2011. For the same period of time 13515 microorganisms/ duplicate were excluded/ were isolated. The evaluation of the resistance of some bacteria to antimicrobial agents is based on the high relative portion which these microorganisms take part in the structure of the bacterial infections and the problems as well, concerning treatment of the infections, caused by them (**Figure 1**). E.coli is the most frequent bacteria causing nosocomial infections. According to our data for 2011 / Bulletin representing the etiological structure and the resistance to antimicrobials of some problematic for hospital infectious pathology bacteria – unpublished official data, as a local issue/ the increasing of the resistance of E.coli strains was registered. – (**Figure 2**); this fact could be explained with the high portion of the strains /22%/ producing extended-spectrum beta-lactamases /ESBL/.

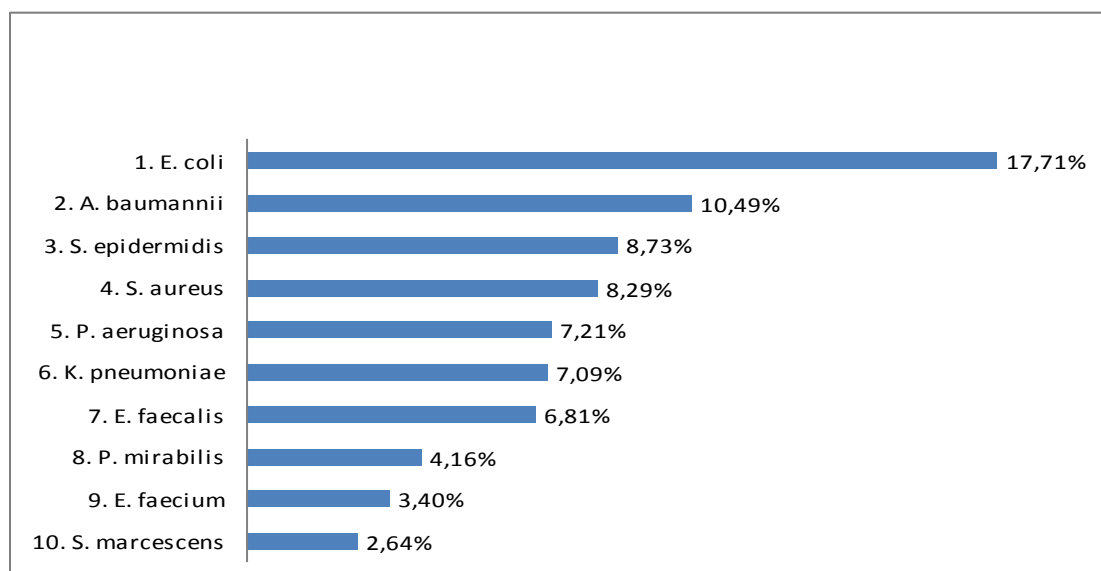


Figure 1. The first ten most often isolated microorganisms - 2011

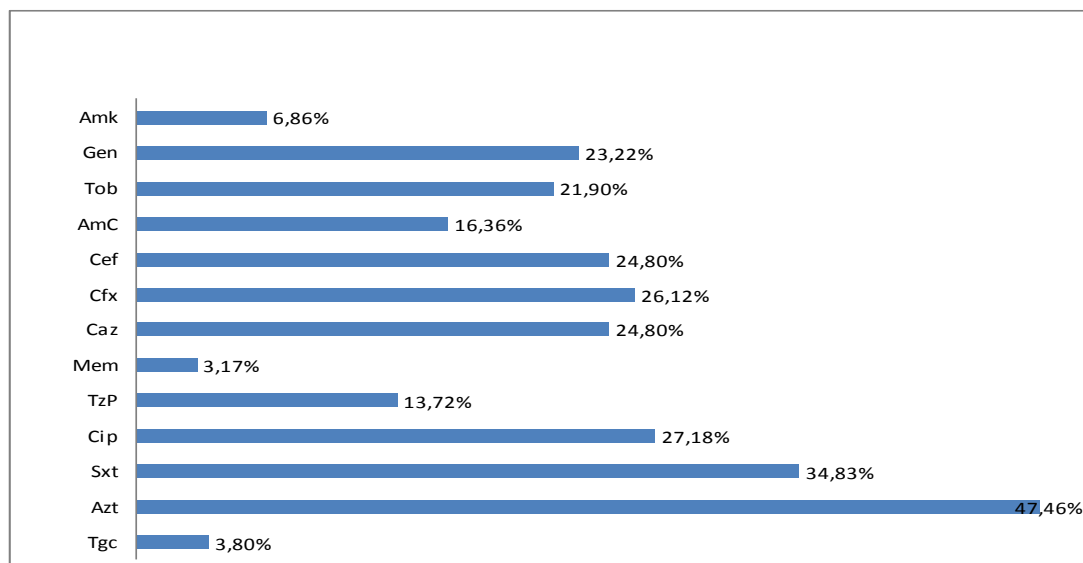


Figure 2. Resistance of *E. coli* to antimicrobials (n=436) - 2011

The same tendency we observed in respect to *Klebsiella pneumoniae* strains, with ESBL production of 72% of the strains investigated. Even worse situation occurs in the *Acinetobacter baumannii* strains. (**Figure 3**). The resistance of this microorganism to carbapenems, to other beta-lactams and quinolones is very high, between 72% and 93%. Also, a problem for our hospital in this respect are multiresistant *P.aeruginosa* strains, *Staphylococcal* strains, particularly resistant to methicillin /oxacillin strains – MRSA, *Enterococcus* spp. (5). On this background, 40.3 Defined Daily Doses per 100 BD were used during 2011 in the MMA hospital. (**Table 1**). Kiivet,R. et al 1998 (6) reported about 41 DDD/100 bed-days used in Tartu University Hospital, Estonia vs. 51 DDD/100 bed-days in Badajoz, Spain and 47 DDD/100 bed-days in Huddinge hospital in Sweden for 1992, three big hospitals in three countries. The data from other hospital in Sofia /Bulgaria/ with 350 beds show antibiotic use in the frame 47.9 DDD/100 bed-days to 61.9 DDD/100 bed-days for 2006-2009 period of time (7). According to Filius,P. et al 2005 (8), the total systemic antibiotic use significantly increased from 47.2 to 54.7 DDD/100 bed-days in Netherlands' hospitals for 5 years period of time (1997 to 2001). The antibiotics used most frequently at MMA were beta-lactam antibiotics with 59.5% or 24 DDD/100 bed-days, of which 13 DDD/100 bed-days are the quantities of the third and fourth generation of cephalosporin and 2.8

DDD/100 bed-days is a relative part of carbapenems. The use of quinolones was 6.1 DDD/100 bed-days and the quantities of aminoglycosides, spent in the hospital were 3.9 DDD/100 bed-days. (**Table 1**). In the Department of General Medicine of a 1100 bedded tertiary care teaching hospital and research center in south India, the third generation cephalosporins were the most commonly prescribed antibiotics – 24.5 DDD/100 bed-days. The aminoglycosides amounts used were 1.82 DDD/100 bed-days, carbapenems 1.36 DDD/100 bed-days, quinolones 8.5 DDD/100 bed-days (9). According to Kiivet,R. et al 1998 (6), the antibiotics used most frequently were tetracyclines and aminoglycosides in Tartu /Estonia/, broad-spectrum penicillins and cephalosporins in Badajoz /Spain/ and narrow-spectrum penicillins and cephalosporins in Huddingein, Netherlands. Shankar,R. et al 2003 (10) reported about 6.1 DDD/100 bed-days of ciprofloxacin, gentamicin 5.14 DDD/100 bed-days, ceftriaxon 4.56 DDD/100 bed-days, metronidazole 10.43 DDD/100 bed-days, used in the Internal Medicine ward of a teaching hospital in Western Nepal during 2002. Nosocomial infections, especially those, occurring with multiresistant bacteria are a major problem in Intensive care unit /ICU/ at MMA. Three bacterial species, *A. baumannii*, *P.aeruginosa* and *K.pneumoniae* accounted for more than 44% of all ICU' isolates.

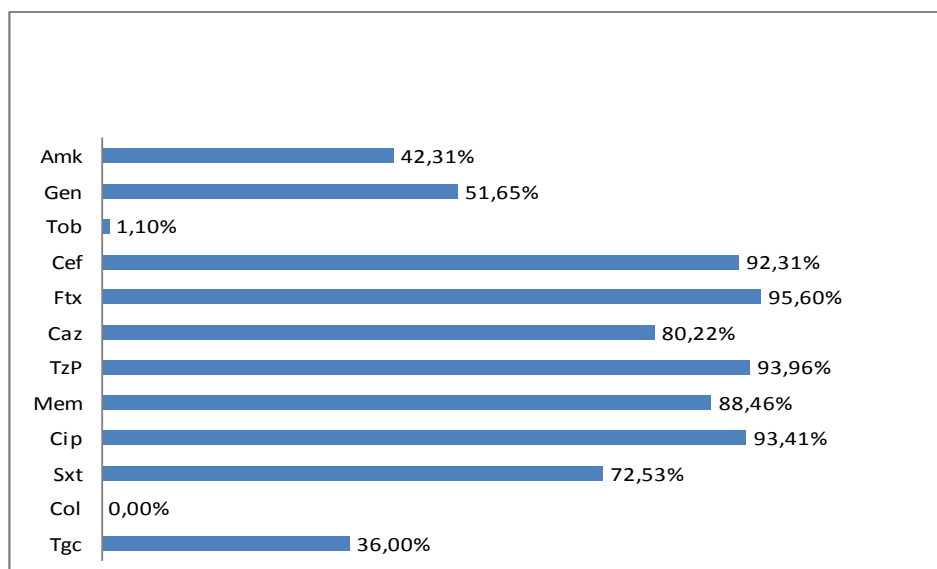


Figure 3. Resistance of *A. baumannii* to antimicrobials (n-192) - 2011

Sxt–sulfam/trimet, **Tob**-tobramycin, **Pip/taz**–piperacilin/tazobactam, **Mem** – meropenem, **Tgc**- tigecyclin, **Gen**–gentamicin, **Col**-colistin, **Cip**–ciprofloxacin, **Caz**–ceftazidim, **Cef**-cefepim, **Amk**-amikacin, **Ctx** - cefotaxim

Table 1. Summary of Defined Daily Doses per 100 Bed Days at MMA for 2011

Antimicrobials	DDD/100BD		
	Hospital	ICU-ARC	Bile-Liver surg. unit
Amoxicillin/clav.acid	0.833	-	-
Ampicillin/ sulbactam	-	31.254	2.214
Piperacillin/tazobactam	0.239	2.546	0.795
Ceftazidim	0.174	-	-
Ceftriaxon	5.671	7.319	13.377
Cefepim	2.979	8.133	9.470
Meropenem	2.214	18.404	12.560
Imipenem	0.598	1.167	10.717
Ciprofloxacin	1.327	-	0.625
Levofloxacin	2.006	-	4.934
Moxifloxacin	1.700	-	-
Vancomycin	0.177	1.236	0.043
Linezolid	0.538	1.919	3.408
Teicoplanin	0.680	0.623	0.666
Aminoglycosides	3.900	19.627	3.430
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Total	40.300	105.2	105.6

The results showed 2.5 fold greater consumption of antimicrobials in our two ICU– 110.9 DDD/100 bed-days and 105.2 DDD/100 bed-days respectively, compared with the hospital as a whole. Very similar data were obtained about Bile-liver surgery clinic /high risk clinic for infection development/ with 105.6 DDD/100

bed-days. Unreasonably large amounts of ceftriaxon have been used in clinics of gastroenterology, bile-liver surgery, traumathology and urology. It is very important, because the third-generation of cephalosporins is the main inductors of ESBL in many bacteria, causing nosocomial infections. Slain,D. et al

2011 (11) reported that in the ICU use in the West Virginia University /USA/ of intravenous ciprofloxacin and ceftazidime declined from 148 and 62.5 DDD/ 1000 patient-days to 40 and 24.5, respectively during 2004 to 2007 and an increase in the use of these agents and resistance to these agents was witnessed during 2008-2010. In the main ICU in St Luke's Hospital, Malta, meropenem was the most antibiotic used with 1997.5 DDD in 2006. (12). According to the same authors, several 3rd. generation cephalosporins were used including ceftriaxon – 629 DDD, ceftazidime – 139.8 DDD and cefotaxime with 49.5 DDD. They also consider that the risk factors associated with carbapenem-resistant *A.baumannii* acquisition include ICU-wide variables, such as the prevalence of ICU colonized patients and ICU' antibiotic overuse.

CONCLUSION

The high level of ESBL producing *E.coli* and *K.pneumoniae* as well as the large relative part of the multiresistant *A.baumannii* and *P.aeruginosa* strains isolated at MMA show the significance of antibiotic' type and quantities used in the hospital. The problem is related to the large quantities expressed as DDD/ /100 bed-days of beta-lactams and more precisely of the 3 rd generation of cephalosporins and carbapenems used not only in ICU, but also in other high risky for infection development units. All the data discussed in this study suggest that nosocomial infections need an improved infection control and the feedback on antimicrobial resistance could be an important tool to start actions against misuse of antibiotics in big hospital complexes and especially in ICU as well.

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