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BACTERIAL PATHOGENS WITH MULTIDRUG RESISTANCE. ETIOLOGICAL STRUCTURE OF INFECTIONS IN ICU, UMBAL-EAD STARA ZAGORA

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ABSTRACT

High prevalence of resistance leads to increased antibiotic prescripting which results in extra costs and further emergence of new resistance mechanisms. In addition, such high prevalence might well contribute to increased morbidity and extra-incidence of nosocomial infections The aim of the present report is to determine the etiological structure of the infections in patients in ICU and their frequency of transmission of MDROs; determination of the mechanisms of phenotypic resistance of the most frequent isolates with epidemiological value.. Our analysis has been performed for the period 2004-2008.We have investigated 1129 different materials. Conventional methods have been used for isolation of bacterial pathogens. The antimicrobial susceptibility testing has been performed by Disk Diffusion Method with different antimicriobial agents. In conclusion, we could say that MDROs are mostly among Gram negative bacilli-P. aeruginosa, E. coli, A. baumannii. E. coli , producing ESBLs are 18%;group KES (Klebsiella, Enterobacter, Serratia), producing ESBLs are 27%. Carbapenems are effective to ESBLs producing Enterobacteriaceae.MRSA are 21%.

Key words: MDROs, MRSA, HLAR, GNFB, VISA

INTRODUCTION

Multidrug-resistant organisms (MDROs) are spreading worldwide. Acquisition of additional resistance genes minimizes therapeutic options and leads to frequent treatment failure. Laboratory diagnostics is laborious and time-consuming and requires combinations of different phenotypic and molecular methods. Increasing knowledge of treatment and diagnostics is essential for physicians. High prevalence of resistance leads to increased antibiotic prescripting which results in extra costs and further emergence of new resistance mechanisms. In addition, such high prevalence might well contribute to increased morbidity and extra-incidence of nosocomial infections (1).The prevention and control of MDROs is a national priority - one that requires that all healthcare facilities and agencies assume responsibility. Successful prevention and control of MDROs requires administrative and scientific leadership and a financial and human resource commitment (2).

MDRO definition. MDROs are defined as microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents (3).These highly resistant organisms deserve special attention in healthcare facilities (4).In addition to MRSA (methicillin-resistant S. aureus) and VRE(vancomycin-resistant enterococci), certain gram negative bacilli, including those producing extended spectrum β-lactamases (ESBLs) and others that are resistant to multiple classes of antimicrobial agents, are of particular concern (2).

Importance clinical of MDROs. Increased lengths of stay, costs, and mortality also have been associated with MDROs (5-10).

Epidemiology of MDROs. Prevalence of MDROs varies temporally, geographically, and by healthcare setting(15, 16). The type and level of care also influence the prevalence of MDROs. ICUs (intensive care units), especially those at tertiary care facilities, may

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have a higher prevalence of MDRO infections than do non-ICU settings (13, 14). Antimicrobial resistance rates are also strongly correlated with hospital size, tertiary-level care, and facility type (15-16).

Important concepts in transmission. Once MDROs are introduced into a healthcare setting, transmission and persistence of the resistant strain is determined by the availability of vulnerable patients, selective pressure exerted by antimicrobial use, increased potential for transmission from larger numbers of colonized or infected patients ("colonization pressure") (17,18); and the impact of implementation and adherence to prevention efforts.

Patients vulnerable to colonization and infection include those with severe disease, especially those with compromised host defenses from underlying medical conditions; recent surgery; or indwelling medical devices (e.g., urinary catheters or endotracheal tubes (19-20). Hospitalized patients, especially ICU patients, tend to have more risk factors than non-hospitalized patients do, and have the highest infection rates (2).

The aim of the present report is to determine the etiological structure of the infections in patients in ICU and their frequency of transmission of MDROs; determination of the mechanisms of phenotypic resistance of the most frequent isolates with epidemiological value.

MATERIALS AND METHODS

Our analysis has been performed for the period 2004-2008.We have investigated 1129 different materials –blood culture, sputum,, transtracheal aspirates, bronchial washings, purulent drainages, urines, urethral catheters, pleural and abdominal fluids and etc. Conventional methods have been used for isolation of bacterial pathogens. Blood culture was investigated by "BACTEC"9050(Becton Dickinson BD). We have isolated and estimated 300 bacterial pathogens. Identification has been performed by routine methods or by "Sceptor" and "Crystal" (Becton Dickinson).The antimicrobial susceptibility testing has been performed by Disk Diffusion Method with different antimicriobial agents-penicillins, amino-glycosides, fluoroqinolones, glycopeptides and etc.We have studied MRSA (methicillin – resistant staphylococcus); VISA (vancomycin-intermediate S. aureus); Enterobacteriaceae, producing ESBL (extended-spectrum β-lactamases); HLAR (high level aminoglycosid resistance) enterococci; staphylococcus and enterococcus resistance to glycopeptides; Enterobacteriaceae resistance to glycopeptides and GNFB (Gram negative nonfermentative bacilli).

RESULTS AND DISCUSSION

When analyzing the frequency of the different resistant organisms in the investigated trials, it has been established that the GNFB predominate, being followed by E. coli, Enterobacter, Klebsiella .The other microorganisms are Staphylococcus, Enterococcus and Candida **(Figure 1)**.

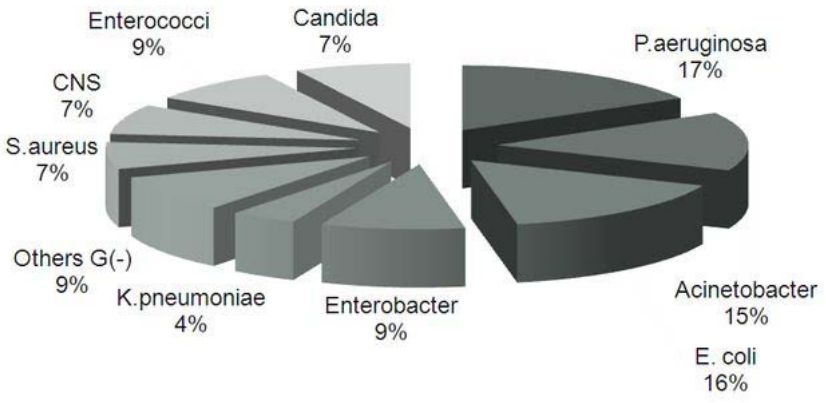

Figure 1. Ethiological structure of infections

When analyzing the resistance among GNFB it has been determined that Pseudomonas aeruginosa strains show high resistance to ureidopenicillins and fluoroquinolones.The resistance to second and third generations cephalosporins is between 18%-23%,while the resistance to aminoglycosides has statistically important difference (Ampicillin 11% and Gentamicin 38%) which imposes restriction in the usage of Gentamicin.As for Acinetobacter baumanii its resistance is even higher, but Ampicillin/sulbactam keeps its activity (**Figure 2)**. On a separate figure the resistance to imipenem in absolute value has been shown **(Figure 3)**.

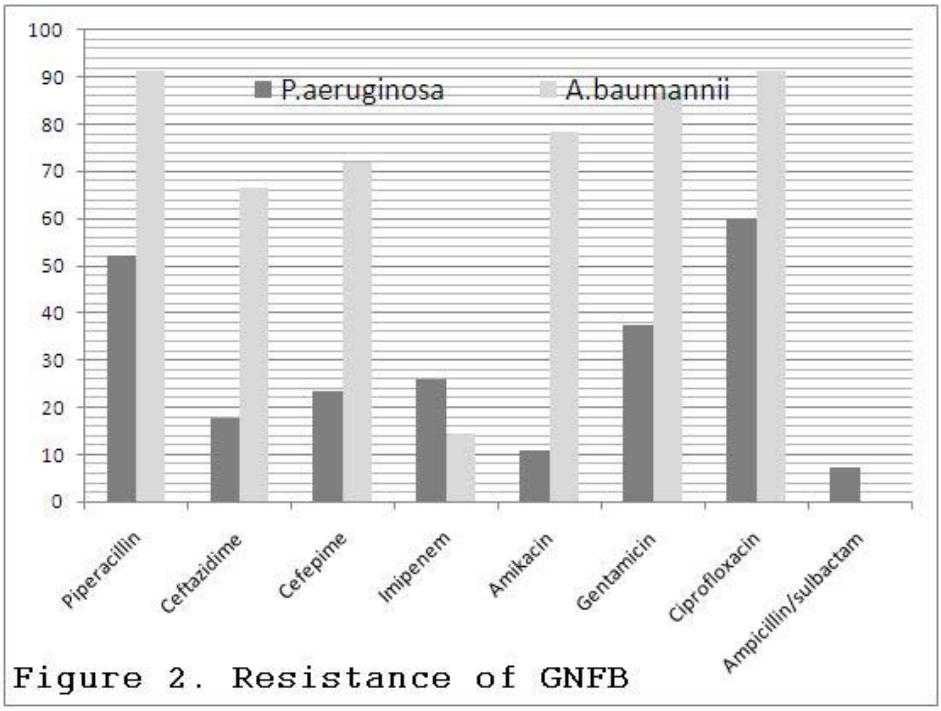

Figure 2. Resistance of GNFB

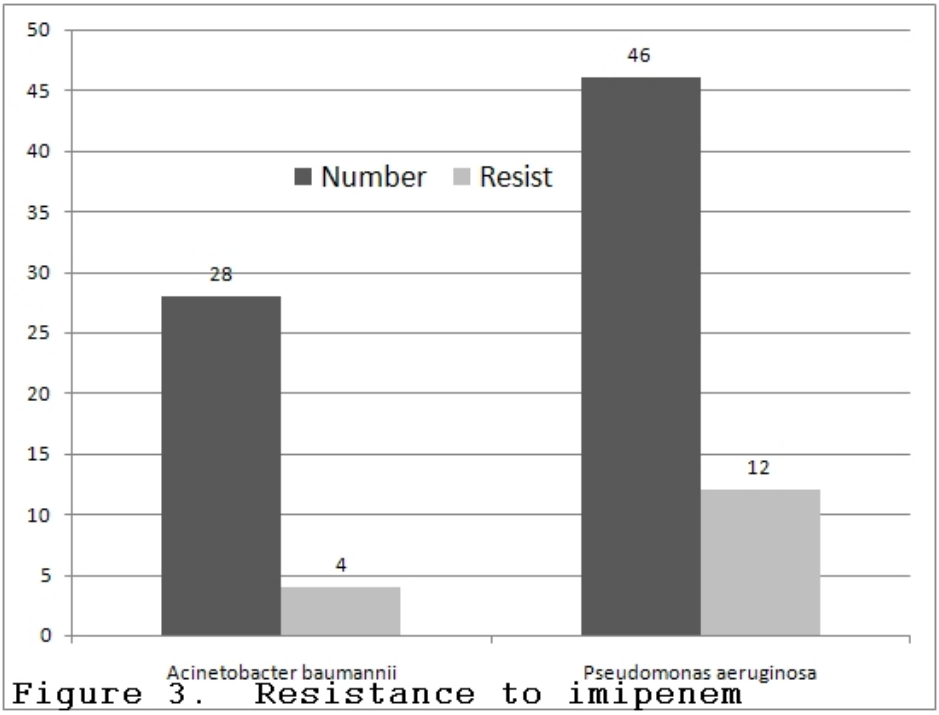

Figure 3. Resistance to imipenem

E. coli and K. pneumonia show resistance to all groups of antibiotics except for imipenem **(Figure 4)**.

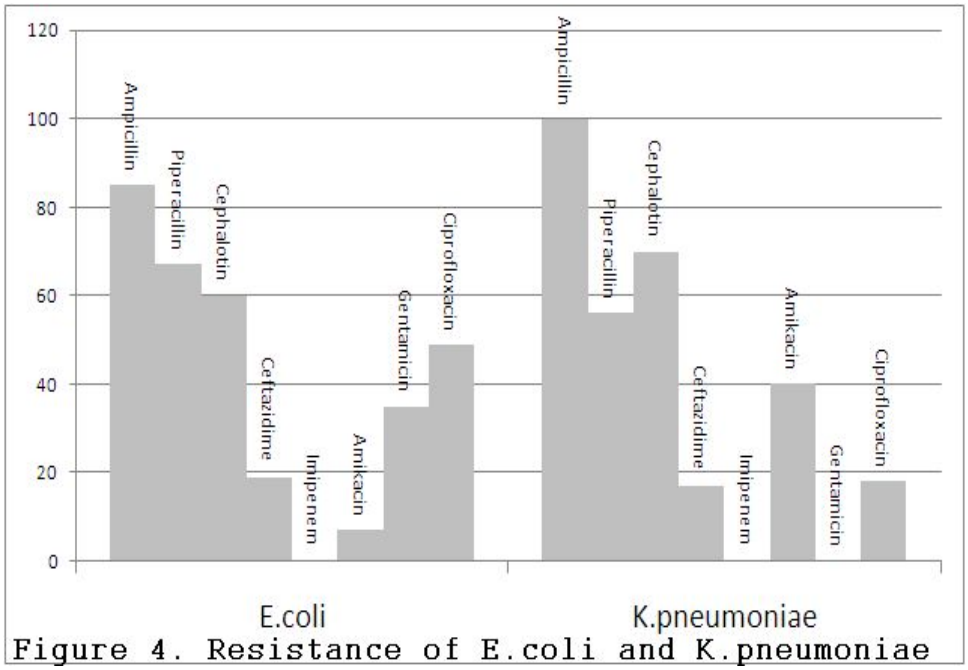

Figure 4. Resistance of E.coli and K.pneumoniae

Ceftazidime is a medicine of choice in the therapy of severe infections caused by MDROs. The highest resistance is observed in Acinetobacter baumannii, followed by E. coli and Enterobacter **(Figure 5)**.

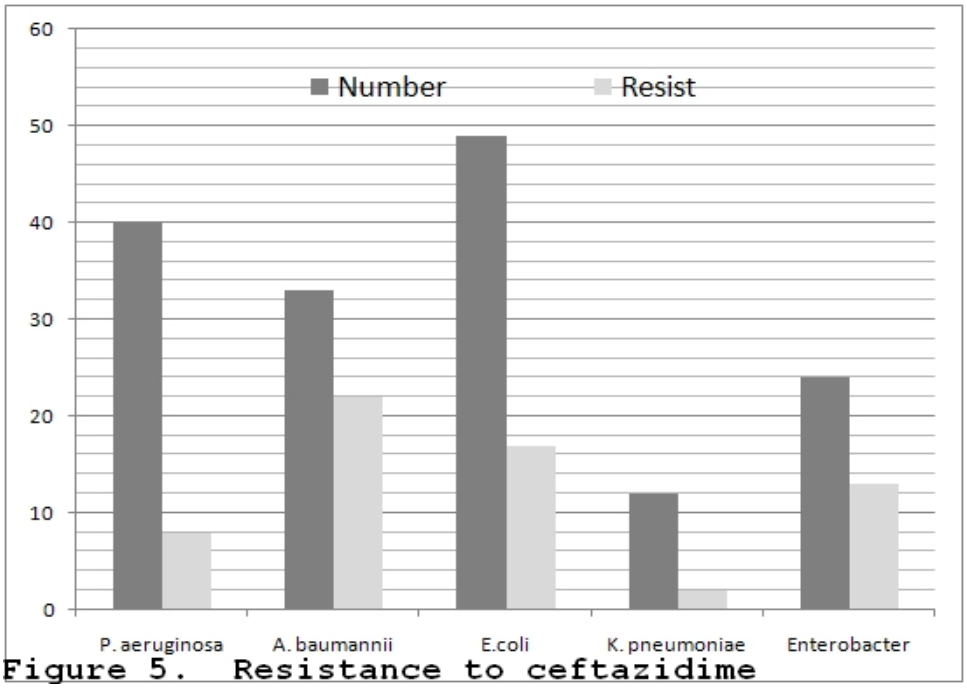

Figure 5. Resistance to ceftazidime

In recent years there has been an increased incidence and prevalence of extended-spectrum β-lactamases (ESBLs), enzymes that hydrolyze and cause resistance to oxyimino-cephalosporins and aztreonam (21). Among the bacteria being tested, the number of K. pneumonia strains, producing ESBL is the highest **(Figure 6)**.

Staphylococcus aureus (MRSA) are 21%, which are proved with Oxacillin screen agar. Treatment of infections caused by methicillin-resistant staphylococci is discussed. Vancomycin is the treatment of choice. Alternatives have been few because methicillin-resistant strains often are resistant to multiple antibiotics in addition to beta-lactam antibiotics. New agents which are active against methicillin-resistant staphylococci are becoming available, and their potential role in treatment is discussed (22). The resistance of the coagulase-negative staphylococci(CNS) is higher.It is connected with the fact they are isolated from blood **(Figure7)**.

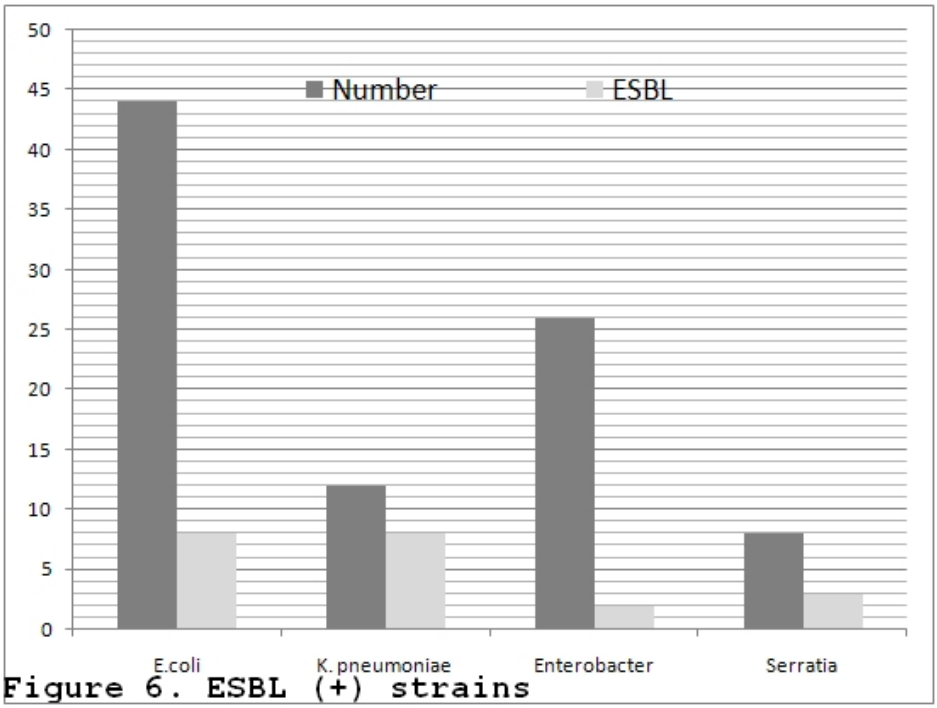

Figure 6. ESBL (+) strains

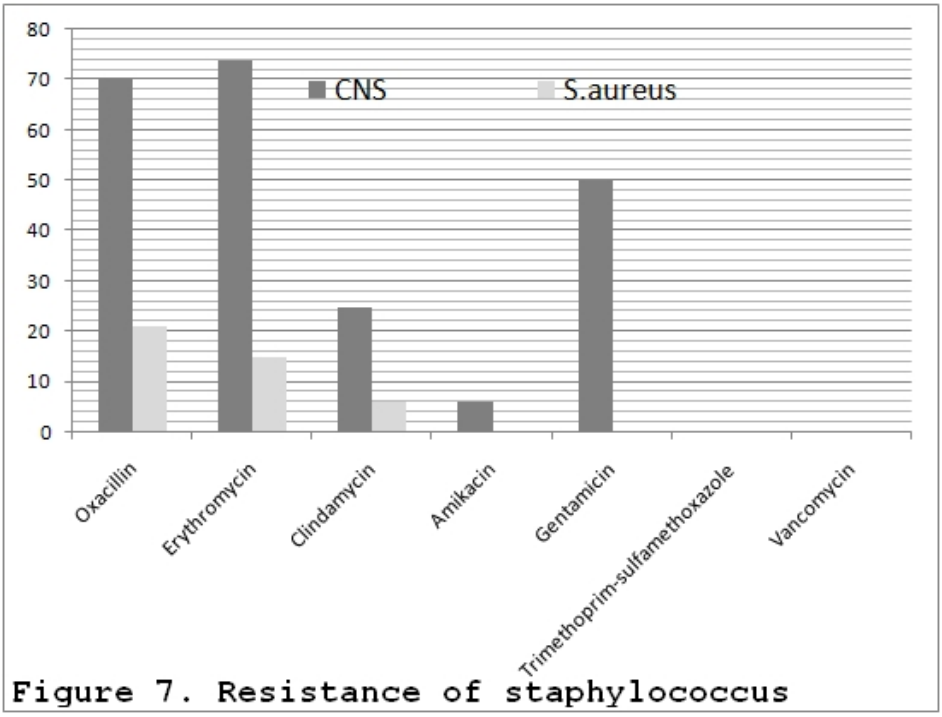

Figure 7. Resistance of staphylococcus

Enterococci have become a vexing problem in clinical medicine because of their ability to infect patients who are typically receiving antibiotic therapy for unrelated underlying illness. Moreover, the infections have become extremely difficult to manage because of the accumulation of antibiotic resistances among enterococci. The ability of enterococci to cause disease is an intrinsic property of the organism or possibly subpopulations within enterococcal species. The probability of an infection's becoming established, however, is almost certainly in part a function of the enterococcal burden. By altering endogenous bacterial flora, antibiotic therapy promotes increased colonization by antibiotic-resistant organisms. Therefore, antibiotic resistance and intrinsic virulence both contribute to disease, but in separate and complementary ways(23).We have determined high resistance to penicillins, aminoglycosides and fluoroquinolones in enterococcus in our investigation. Resistance to vancomycin has not been established **(Figure 8)**.

CONCLUSIONS

In conclusion, we could say that MDROs are mostly among Gram negative bacilli-P. aeruginosa, E. coli, A. baumannii. E. coli , producing ESBLs are 18%;group KES (Klebsiella, Enterobacter, Serratia), producing ESBLs are 27%. Carbapenems are effective to ESBLs producing Enterobacteriaceae.MRSA are 21%.

MDRO Prevention and Control

Prevention of Infections. Preventing infections will reduce the burden of MDROs in healthcare settings. Prevention of antimicrobial resistance depends on appropriate clinical practices that should be incorporated into all routine patient care. These include optimal management of vascular and urinary catheters, prevention of lower respiratory tract infection in intubated patients, accurate diagnosis of infectious etiologies, and judicious antimicrobial selection and utilization.

MDRO surveillance. Surveillance is a critically important component of any MDRO control program, allowing detection of newly emerging pathogens, monitoring epidemiologic trends, and measuring the effectiveness of interventions(2).

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