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ANTIMICROBIAL THERAPY AND CLOSTRIDIUM DIFFICILE INFECTION

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ABSTRACT. The study intends to evaluate antibiotic therapy in *Clostridium difficile* infection (CDI) in order to determine infection fatality risk rates depending on patient's age and type of antibiotic therapy, assuming that those over 60 years old with broad spectrum cephalosporins and quinolones regimens are under aggravating risk factors. A number of 71 CDIs were analyzed of the 183 nosocomial infections registred in Arad Emergency Hospital taking into account patient age, previous admissions, contact with other ICD cases, prior antibiotic treatment and cases evolution. Gram positive bacteria have caused 52.5% of nosocomials, most of them assisted on surgical (17,7%), infectious diseases (15,6%,) and intensive care units ATI (12,5%). Most of them were enterocolitis (40,4%), urinary tract infections (21,8%) and nosocomial pneumoniae (16,1%). The CDI patients'average age was 67 years (extreme 20-88 years, Std.dev.14, 69). The gender ratio was F: M = 1.53, with fatal evolution for 12.7% of cases, the relative risk of death being 2.2791 for female patients. Broad-spectrum cephalosporins were given in 52.11% of cases and the relative risk for adverse outcome in patients over 60 years with ICD associated with third generation cephalosporins treatment was 17.6333 (P = 0.0430, 95% CI 1.0952 to 83.9138). CDI is the first cause of nosocomials in 2016 for Arad Emergency Hospital, being encouraged by broad-spectrum cephalosporins therapy in over 60 years old patients.
KEYWORDS: nosocomial, Clostridium difficile, cephalosporins

INTRODUCTION

Nosocomial infections are ubiquitous in medical practice, with regulated registration but with poor reporting from hospitals at all levels. Until 2010, the responsible involved germs were mainly *Acinetobacter baumannii, Klebsiella spp, Proteus spp, E. coli, Pseudomonas aeruginosa, Staphylococcus aureus,* recent years being dominated by *Clostridium difficile*.(1, 2, 3)

"In 2013, although only a small number of hospitals in Romania have assured the CDI's etiological laboratory diagnosis, preliminary data showed presence and increased frequency of disease (1237 reported cases). Microbiological reports, evaluated in a pilot study in 10 hospitals in Romania, revealed a significantly increased prevalence and characteristics of PCR ribotype 027 strains of *Clostridium difficile,* which is being known as a highly epidemiogenic strain (with increased transmissibility, sporulation and producing of specific A and B) and also being responsible of the production of additional binary toxin, correlated with increased disease severity and higher rates for relapse "(1,5, 6)

Exposure to *Clostridium difficile* can result in various conditions from asymptomatic carrier status to medium and severe forms of acute enterocolitis, even pseudomembranous colitis too (2, 4, 7, 8).

In the first 30 days of symptomatic infections rate mortality can reach 9-38% of the cases[3]; excesses in antibiotics regimens have led to increased burden of this disease, especially in over 60 years old patients. .(9, 10, 11, 12)

The study objective is to establish the risk of *Clostridium difficile* infection in over 60 years old patients who received treatment with broad-spectrum cephalosporins.(13,14,15,16).

MATERIAL AND METHODS

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Of 193 nosocomials were analysed 71 CDI's which were assisted in Arad Emergency Hospital in 2016, by age, gender ratio, previous addmitance and contact with other CDI's patients, previous antibiotic regimens and cases outcome. Data were *IBM SPSS Statistics 20* and *MedCalc* processed for rates, ratios, variances, correlations and relative risks for unfavorable outcome.

RESULTS

Ten nososcomials have had unknown or viral etiology (5,18%) and 183 had been documented with bacterial etiology.

Gram positive bacteria have caused 52,5% od the infections, most of them being assisted in surgical wards (17,7%), adult infectious diseases ward (15,6%,) and Intensice Care Units ICU's (12,5%).

Gram negative bacteria were predominant in ICU's (43,6%) and neurology ward (41,3%). Their wards distribution was statistically significant in these departments, $P < 0,0001$, Table 1.

Ward/department	% Gram negative	% Gram positive
ICU	43,67	12,5
Adult infectious diseases	0	15,62
Cardiology	0	3,12
Surgery	3,44	17,70
Diabetes	0	1,041
Gastroenterology	0	6,25
Hematology	0	3,12
Internal medicine	1,14	1,041
Nefrology	0	8,33
Neurology	41,37	6,25
New born	2,29	2,083
Obstetrics gynecology	1,14	7,29
Orthopedy	3,44	2,083
Palliative	3,44	3,12
Pneumology	0	9,37
Coronary ICU	0	1,041

Table 1 Gram positive and negative bacteria distribution in hospital departments

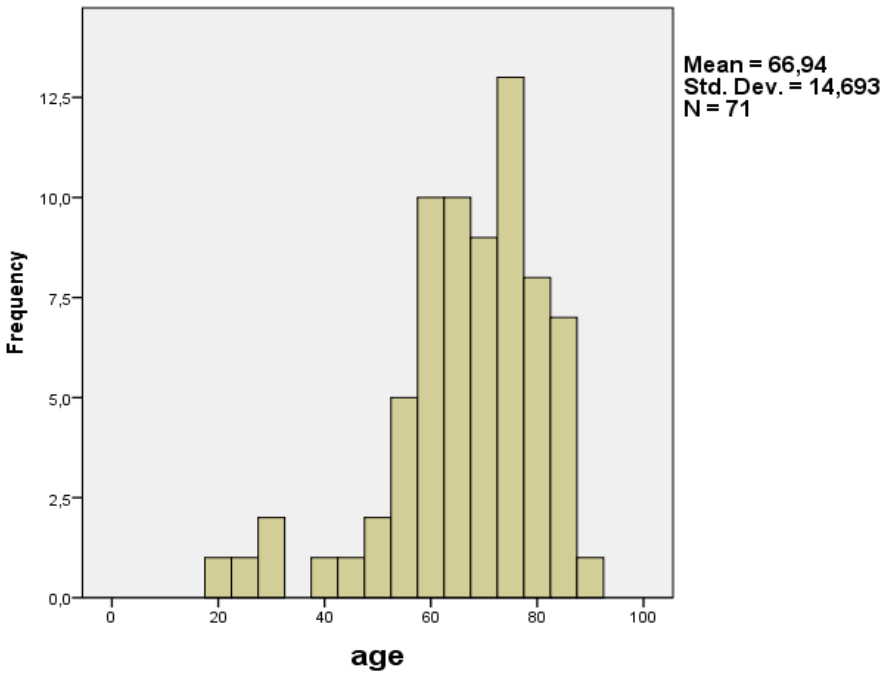
Most of them were enterocolitis (40,4%), urinary tract infections UTI (21,8%) and Hospital-acquired pneumonia HAP (16,1%).

ICU's have assisted the entire nosocomial sepsis cases, 87% of all bronchopneumonia, 83% of pneumonia and 28% of wound infections, compared to other wards , Table 2 .

% infections	ICU	Other department
Blood infection	100	0
Bronchopneumonia	87,5	12,5
Pneumonia	83,87	16,12
Wound infections	28,57	71,42
Enterocolitis	7,69	92,3
Urinary tract infections	2,38	97,61

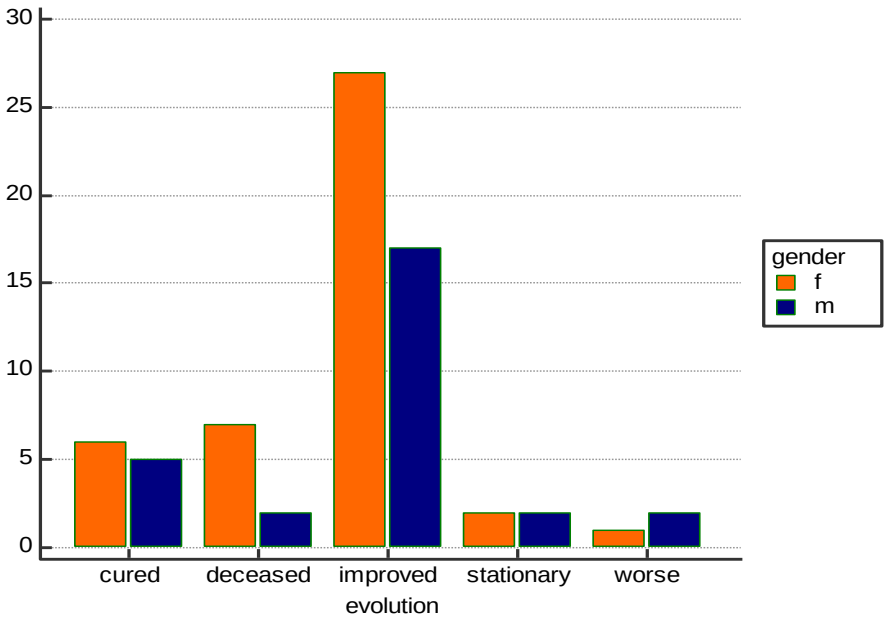
Table 2 ICU infections compared to other hospital departments

Clostridium difficile infection represented 38% of all nosocomials.
Gender Ratio was F : M= 1,53.
CDI's average patients age was 67 (extreme 20-88 years, Std.dev.14,69). Graphic 1.



Graphic 1 - CDI's patient age histogram

Favourable outcome represented 75% of causes și fatality was registred in 12,7% of cases, relative risk for death being 2,2791 pentru female patients compared to male. Graphic 2.



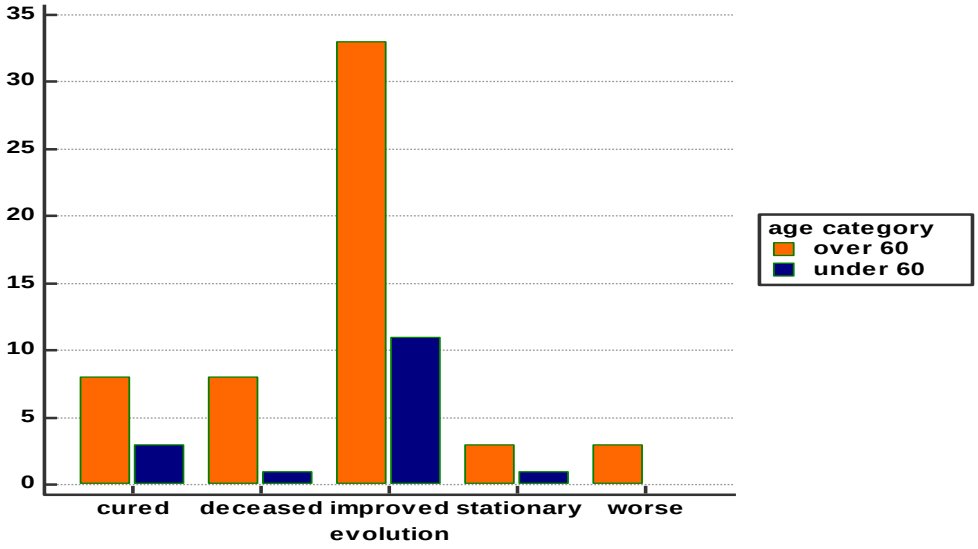
Graphic 2 - CDI's gender distribution for outcome

CDI was present at addmitance in 14 cases (20%) and other 5 cases have relapsed (7%).

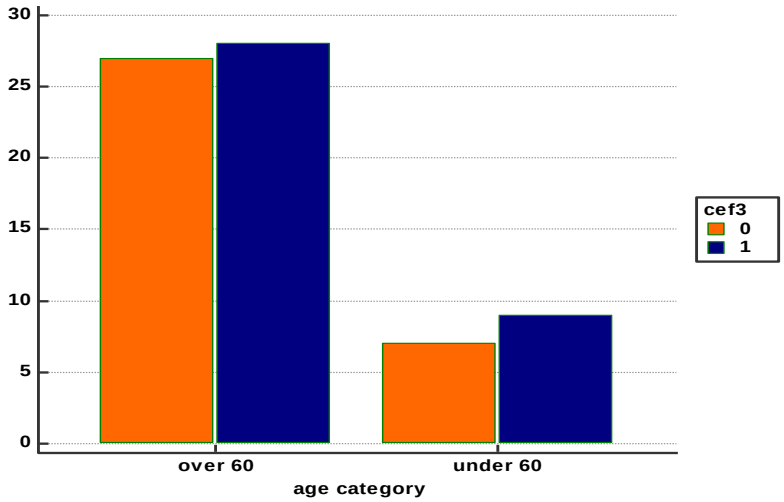
CDI patients with immunosuppression phenomena were a majority, 45 (63%), deceased rate being also extremely high, with death risk of 23,11 (95% CI 3,3352 to 160,1455, P = 0,0015) compared to others.

Antibiotic regimen in patients' recent history was documented in 64 cases (90%) and 56 of them (87%) have received quinolones and broad-spectrum cephalosporins.

Third generation cephalosporins were exclusively prescribed in 52,11% of cases and unfavorable outcome relative risk in over 60 years old patients receiving these prescriptions was 17,6333 (P = 0,0430, 95% CI 1,0952 to 83,9138).

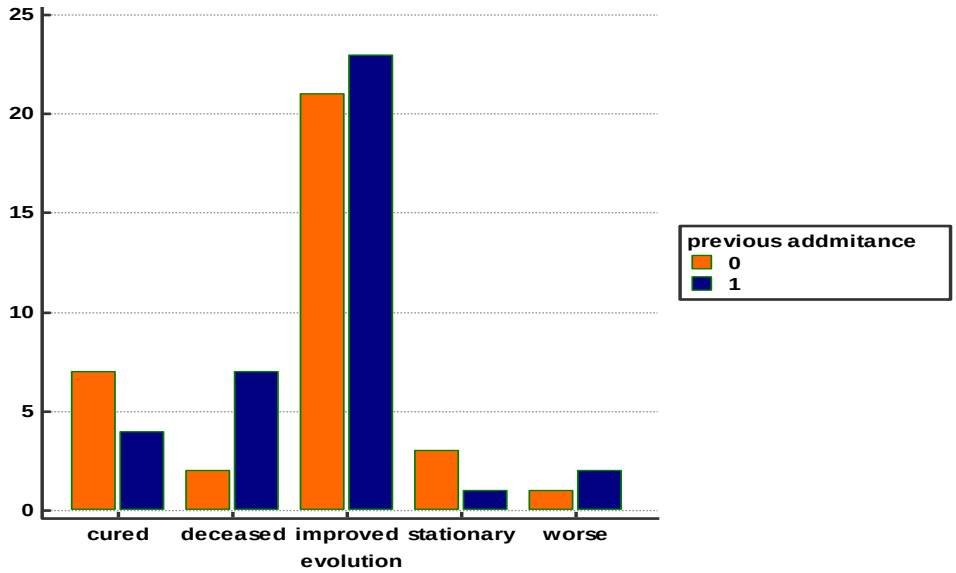


Graphic 3 - CDI's age-related outcome



Graphic 4 - CDI's age-related Third generation cephalosporins treatment

Previous addmitance has played an important role in cases' evolution, 78% of deaths being present in frequently hospitalised patients. Graphic 5



Graphic 5 - CDI's outcome previous addmitance's related

DISCUSSION

CDI is the first cause of acute enterocolitis associated to hospital addmitance and treatment in the world [4],

In our study we found that the CDI being the first cause for nosocomials in 2016 for Arad Emergency Hospital 's over 60 years old patients which were prior treated extensively with broad-spectrum cephalosporins.

They are to avoid broad-spectrum antibiotics, especially in elder.

Contact healthcare professionals with CDI's patients must be reduced until symptoms resolve. Full protective equipment, including gloves, should be worn by all in contact with these patients, including visitors. Hand hygiene is required.

Suspected or confirmed CDI's patients have to be placed in isolation room. If possible, the patient will receive dedicated and exclusive equipment and medical instruments.

Surface disinfection with chlorine products will be done with dedicated equipment and cleaning utensils as well.

CONCLUSIONS

Probiotics have not been shown to be effective in CDI 's prevention. CDI was the first cause of nosocomials in 2016 for Arad Emergency Hospital. This situation was sustained by the broad-spectrum cephalosporins therapy in over 60 years old patients. For CDI preventing each hospital must build a program to decrease the incidence of disease among its patients.

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