

CLOSTRIDIUM DIFFICILE INFECTION - ANALYSIS OF RISK FACTORS IN CONSTANTA

Hangan Aurelia^{1,2}, Dumitru Eugen^{1,2}, Rugina Sorin^{2,3,4}, Dumitru Irina Magdalena^{1,2}

¹ Faculty of Medicine, Ovidius University of Constanta, Romania

² Clinical Infectious Diseases Hospital Constanta, Romania

³ Academy of Medical Sciences

⁴ Romanian Academy of Scientists

Irina Magdalena Dumitru

email: dumitruir@hotmail.com

phone: +40744761297

ABSTRACT

It has been estimated that the human gut contains about 1,000 species of bacteria and 100 times more genes than are found in the human genome. Over 2 Kg - as weight. It is the human microbiom that form a true "forgotten organ" of our body.

Due to the abuse of antibiotics, the Clostridium difficile infection became one of the top nosocomial infections due to complications and financial pressure on the medical system.

We conducted a prospective study of the characteristics of risk factors and epidemiological aspects in patients with Clostridium difficile infection admitted to the Clinical Hospital for Infectious Diseases from Constanta for a period of 3 years. Demographics (age), risk factors (surgery, history of antibiotics or proton pump inhibitors, comorbidities) were noted. The classes of antibiotics used, other than the basic treatment of the condition were analyzed. Also the source of the infection including the ward where the patient was previously hospitalized.

47% (104) of the patients were in the 60-80 interval of age. Nearly half of the patients had a history of surgery. Only 52 patients out of a total of 221 had no history of antibiotic therapy. More than half had PPI therapy prior to the onset of CD infection. In terms of comorbidities, they are multiple, at different systems, the most common being cardiovascular, nutritional and renal diseases. The source of infection was found as nosocomial in 65% of patients. Regarding the origin of the hospital wards, the surgical departments were the main ones in which CD infections appeared: General Surgery (46), Orthopedics (33) and Urology (13).

Our study results confirm that reported risk factors are advanced age, antibiotics use, proton pump inhibitors administration, comorbidities and exposure to health care system.

Keywords: Clostridium Difficile, recurrence, risk factors, human microbiom

Introduction

The main protection against CDI is the normal integrity of the intestinal microflora (1).

Age over 65 years old, prolonged hospitalization and antibiotic treatments are the main risk factors for CDI (2).

After the age of 65, the risk of CDI increases 5 to 10 times (3).

Clostridium difficile is the leading cause of infectious diarrhoea in hospitalized patients (4).

These infections lead to prolonged hospitalizations, increased morbidity and mortality, and high health care costs.

Materials and Methods

The current study concerns the epidemiological aspects on a group of 221 patients with enterocolitis with Clostridium Difficile hospitalized in the Clinical Hospital of Infectious Diseases Constanta.

The study is prospective, lasting 3 years, using inclusion and exclusion criteria and a form for collecting the information considered necessary.

Inclusion criteria:

- adult patients over 18 years of age
- with diagnosis at discharge of diarrhea with Clostridium Difficile

- with bacteriological tests positive for CD (toxins, cultures) or negative but in the presence of a high clinical suspicion.

Exclusion criteria:

- patients under 18 years of age
- with a diagnosis of diarrhea of unspecified or specified etiology other than *Clostridium difficile*.

Data were collected (analytical file) on risk factors: age > 60 years, contact with the health system, surgery, previous antibiotic therapy, comorbidities, the infection origin, the ward of the previous hospitalization.

Results:

Most patients were in the 60-80 age group (47%). Age over 60 is considered a risk factor for *Clostridium difficile* infection.

In 106 patients we find a recent surgery (less than 3 months).

The most common antibiotics incriminated were cephalosporins (52), fluoroquinolones (48), other betalactams (35).

The most common comorbidities were cardiovascular (67), nutritional (47) and renal (44) diseases.

The source of infection was found to be nosocomial in 145 of the patients (65%), 73 (33%) in the community.

The wards origin in most cases were General Surgery (46), Orthopedics (33), Urology (13) followed by the medical departments of Internal Medicine (10), Pulmonology (10) and Infectious Diseases (8).

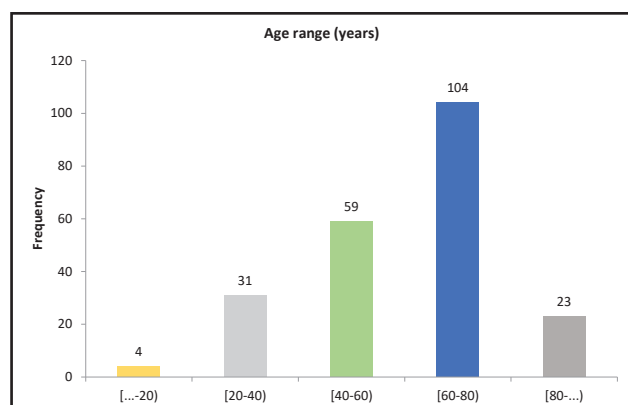


Figure 1 The distribution of patients analyzed according to age at diagnosis

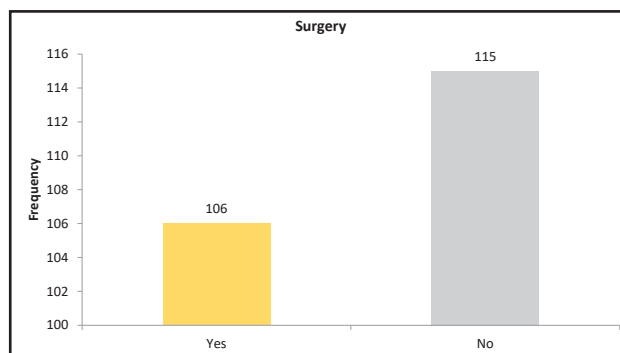


Figure 2 Distribution of patients according to surgery as a risk factor

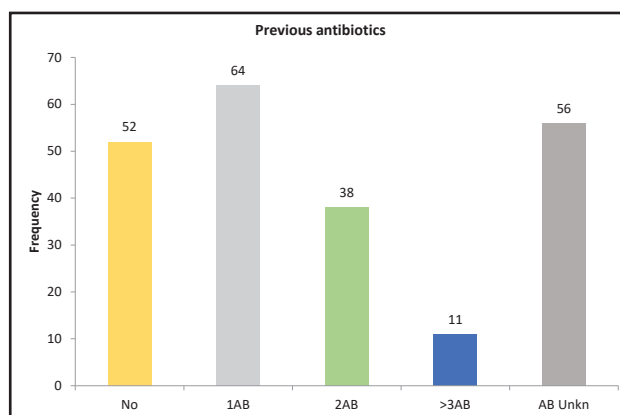


Figure 3 Distribution of patients according to use of antibiotics as a risk factor

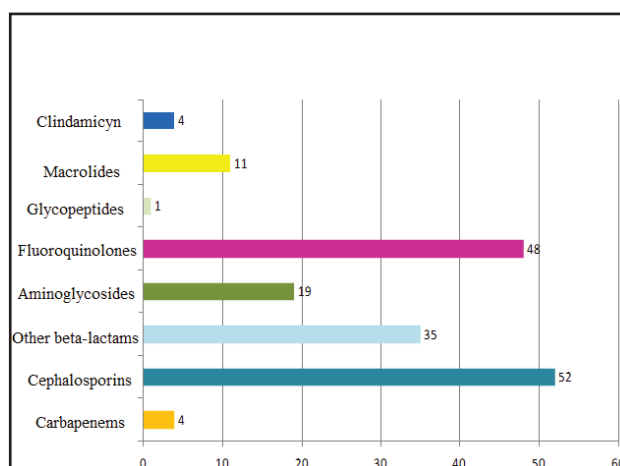


Figure 4 Distribution of patients according to use of different classes of antibiotics as a risk factor

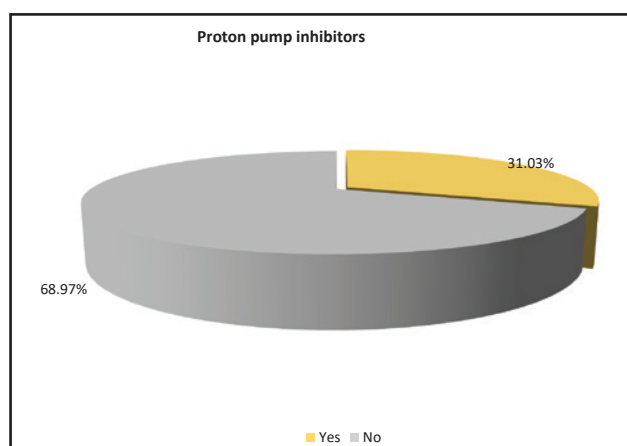


Figure 5 Distribution of patients according to use of proton pump inhibitors as a risk factor

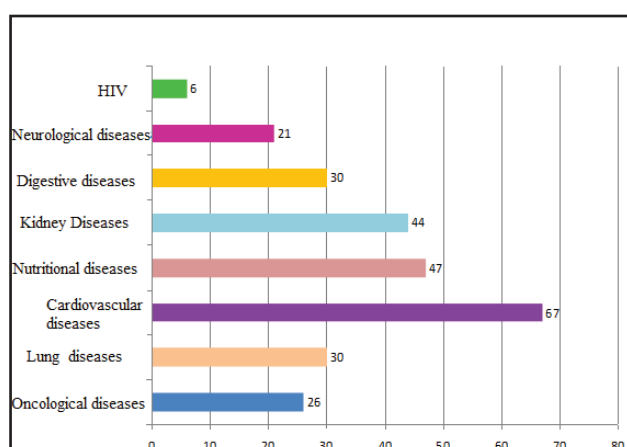


Figure 6 The distribution of patients analyzed according to comorbidities at diagnosis

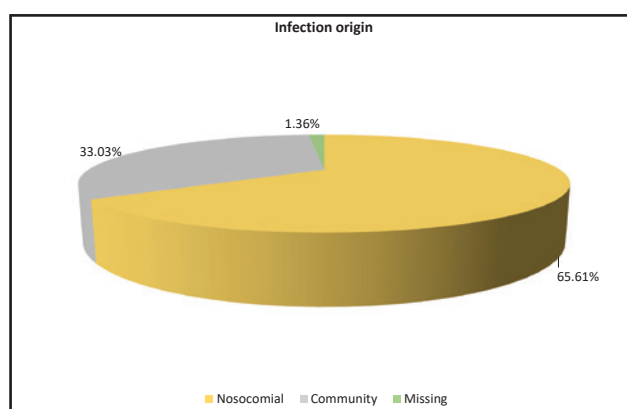


Figure 7 Repartition by the source of the infection

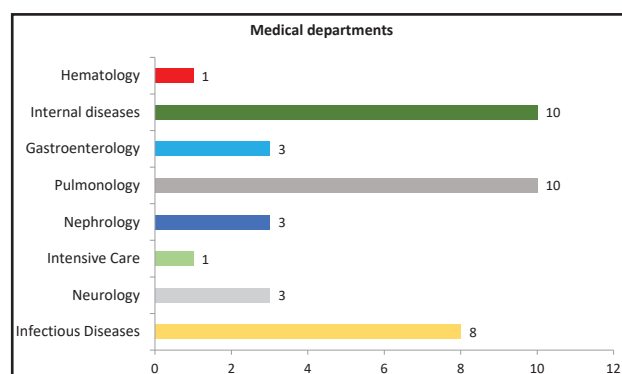


Figure 8 Repartition by wards origin of the infection

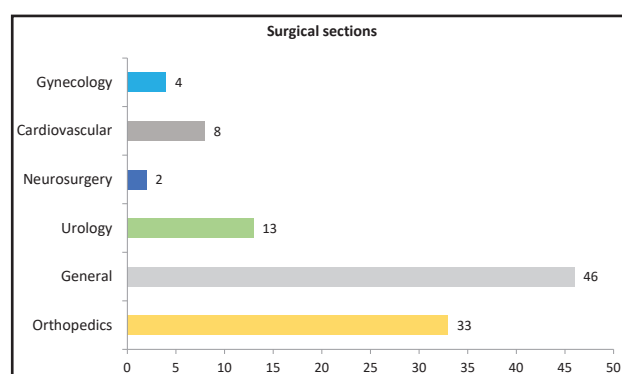


Figure 9 Repartition by wards origin of the infection

Discussions:

The primary requirement for the expression of the pathogenicity of toxigenic strains of *C. difficile* is a change in the normal relations of the bacteria colonizing the digestive tract, which constitute a barrier to the proliferation of pathogenic microorganisms. More than 90% of infections caused by *C. difficile* occur upon the administration of antibiotics. The effects of antibiotics disrupt the normal flora of the colon, allowing endogenous and exogenous microorganisms (*C. difficile*) to proliferate and colonize the colon (5,6).

According to data from previous studies, 70-90% of diseases caused by *C. difficile* develop after the administration of antibiotics (4,7).

Most studies that evaluated CDI showed that older patients (especially those over 60) had the highest risk of developing CDI. In a study by Al-Eidan et al (8) 87 of their hospitalized patients with CDI had severe underlying diseases and the presence of two or more simultaneous diseases was found in 21 patients (24.1%). Also in their study, Kyne et al. (9) found that CDAD was

associated with severe comorbidities (OR = 17.6; 95% C.I. = 8.8-53.5).

Conclusions

Our study highlighted that several risk factors for the development of CDI were identified (old age, applied antibiotic therapy and proton pump inhibitors, surgery, comorbidities, recent stay at a hospital).

Because CDI outbreaks are often multifactorial in terms of cause, the prevention and control of outbreaks must involve multiple interventions aimed at improving antimicrobial use across the health care system and in individual patients (10).

References

1. Smits WK, Lyras D, Lacy DB, Wilcox MH, Kuijper EJ. Clostridium difficile infection. *Nat Rev Dis Prim*. 2016 Apr;2:16020.
2. Czepiel J, Drózd M, Pituch H, Kuijper EJ, Perucki W, Mielimonka A, et al. Clostridium difficile infection: review. *Eur J Clin Microbiol Infect Dis* Off Publ Eur Soc Clin Microbiol. 2019 Jul;38(7):1211–21.
3. Czepiel J, Kędzierska J, Biesiada G, Birczyńska M, Perucki W, Nowak P, et al. Epidemiology of Clostridium difficile infection: results of a hospital-based study in Krakow, Poland. *Epidemiol Infect*. 2015 Nov;143(15):3235–43.
4. Campbell KA, Phillips MS, Stachel A, Bosco JA 3rd, Mehta SA. Incidence and risk factors for hospital-acquired Clostridium difficile infection among inpatients in an orthopaedic tertiary care hospital. *J Hosp Infect*. 2013 Feb;83(2):146–9.
5. Predrag S. Analysis of risk factors and clinical manifestations associated with Clostridium difficile disease in Serbian hospitalized patients. *Brazilian J Microbiol* [publication Brazilian Soc Microbiol. 2016;47(4):902–10.
6. Predrag S, Branislava K, Miodrag S, Biljana M-S, Suzana T, Natasa M-T, et al. Clinical importance and representation of toxigenic and non-toxigenic Clostridium difficile cultivated from stool samples of hospitalized patients. *Brazilian J Microbiol* [publication Brazilian Soc Microbiol. 2012 Jan;43(1):215–23.
7. Cho SM, Lee JJ, Yoon HJ. Clinical risk factors for Clostridium difficile-associated diseases. *Brazilian Journal of Infectious Diseases*. 2012;16(3):256–61.
8. Al-Eidan FA, McElnay JC, Scott MG, Kearney MP. Clostridium difficile-associated diarrhoea in hospitalised patients. *J Clin Pharm Ther*. 2000 Apr;25(2):101–9.
9. Kyne L, Sougioultzis S, McFarland L V, Kelly CP. Underlying disease severity as a major risk factor for nosocomial Clostridium difficile diarrhea. *Infect Control Hosp Epidemiol*. 2002 Nov;23(11):653–9.
10. Owens Robert C. J, Donskey CJ, Gaynes RP, Loo VG, Muto CA. Antimicrobial-Associated Risk Factors for Clostridium difficile Infection. *Clin Infect Dis*. 2008;46(Supplement_1):S19–31.