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Full Length Research Paper

Clostridium difficile infection- an overview on recurrences over two years

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Introduction: Clostridium difficile infection (CDI) is the leading infectious cause of antibiotic-associated diarrhea. The annual rate of the recurrences can be over 100.000 cases and the costs per episode can be over 10.000 euros. Despite the prevention programs implemented in many countries, the rate of the infection continues to increase Purpose: The aim of the study was to evaluate the rate of recurrence of CDI in the patients admitted in "Sf Parascheva" Infectious Diseases Hospital from Iasi, Romania over a period of 2 years (January 1st 2017 to December 31st 2018). Results: Of all the patients addmited in our hospital for CDI in 2017 and 2018, 30,56% were hospitalized for the recurrence of the infection. After analyzing the number of recurrence of the infection 64,89 % of the patients were at the first recurrence, over 19% had a second recurrence of the CDI and the rest, had a 3rd to 6th recurrence. Conclusion: CDI is still a big problem that causes a major burden on the healthcare system and also on the patient. Over 65% of the patients included in the study presented for the first recurrence of CDI, and the rest for second to sixth episode.

Keywords: Clostridium difficile infection, recurrence, treatment

INTRODUCTION

One of the most common causes of nosocomial diarrhea is *Clostridium difficile* infection (CDI) which increases mortality and morbidity in hospitalized patients (Khanna and Pardi 2010). Clinical symptoms of CDI can start from asymptomatic carrier to mild and severe diarrhea, which can lead to fulminant colitis, toxic mega colon, bowel perforation, sepsis, and ultimately death (Nitsan et al., 2018).

Approximately 25% to 33% of antibiotic-associated diarrhea and 90% of pseudomembranous enteritis are caused by CDI (Evans and Safdar 2015).

Although there are guidelines for diagnosis and treatment ofCDI, the rate of the infection continues to increase in Europe and United States. It is a known fact that there has been an enormous worldwide increase in the incidence and severity of CDI over the past 2 decades despite the prevention programs implemented in many countries (Nitsan et al., 2018). A wide range of CDI costs in

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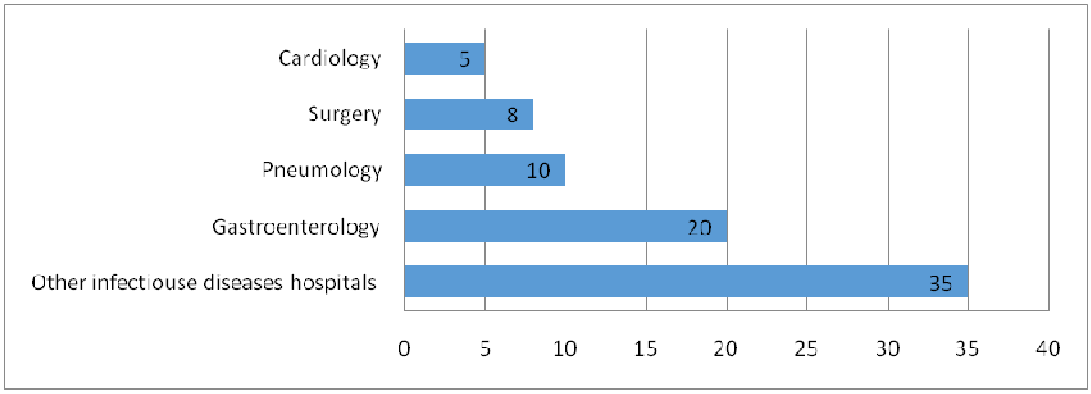


Figure 1 Distribution of medical specialties

Europe have been reported ranging from 5790 euros to 11,202 euros per episode. (Lessa et al., 2015) and the annual rate of RCDI is between 75,000 to 175,000 cases (Shields et al., 2015).

Major risk factors for CDI in the general population are well known and they include exposure to antibiotics (O'Donoghue and Kyne 2011), usage of proton pump inhibitors (PPIs), previous and prolonged hospitalizations, (Kwok et al., 2012; Loo et al., 2011), chemotherapy, immuno compromised states, advanced age (Meyer et al., 2004).

Studies showed that the risk for recurrence after the first episode of CDI is between 20to 35% and, of these, 40–60% will have a second recurrence (Roy et al., 2018).

The evolution of the infection is dictated by the individual characteristics of the patient (risk factors, associated diseases) and the speed and accuracy of the treatment (Ioana and Carmen 2018).

The recurrences of CDI reduce the quality of life and also can place a major burden on healthcare system.(16)Also the social burden that comes with CDI can put the patient in a low psychological state.

MATERIAL AND METHODS

We conducted an observational retrospective study to patients admitted to the "Sf.Parascheva" Infectious Diseases Hospital for a period of one year (January 1st 2017 to December 31st 2018) . The study group was formed from 615 patients diagnosed with CID. '

We analyzed the anamnestic data and all the previous admittances in the hospital and we included in our study188 patients that declared/ were previous admitted for CDI.

Data about the number of the recurrence, associated diseases, days of hospitalization, the presence or absence of the specific toxins, administrated treatment, and if they were transferred from another hospital were taken from the observation sheets of the patients.

RESULTS AND DISCUSSION

Of all 615 patients addmited in our hospital for CDI in 2017 and 2018 , 30,56%were hospitalized for the recurrence of CDI. The age of the patients varies from 15 to 90 years old, with a median of 62. There has been a predominance of female gender, as well as people from urban areas.

Analyzing the number of recurrence of the infection 64,89 % of the patients were at the first recurrence, 18,61% had a second recurrence of the CDI, 16,5% had a 3rdto 6threcurrence.

In 78 (41,48%) cases, the recurrence of the infection occurred in another medical department, fact that required transfer to our hospital. We observed a large addressability from other small hospitals of infectious diseases in the territory, gastroenterology, pneumology, surgical and cardiology departments. (figure.1).

Associated comorbidities, these are represented in figure. 2. Leading pathologies are cardiovascular, and metabolic followed by the hepatic and gastroenterological diseases. Associated pathologies represent risk factors of the disease, aggravating the progression and prolonging hospitalization (Carmen et al., 2012; Ioana and Carmen 2018).

Analyzing the number of days that the patients were hospitalized, in majority of the cases, patients required more than 10 days of hospitalization, with an average of 11 days (figure 3). The prolonged hospitalization increases the medical burden and also adds a psychological and social burden to the patient.

Studies showed that the majority of relapses are due to recurrences of CDI with the original strain, rather than re-infection with a different strain. The management of an initial CDI recurrence includes repeat administration of

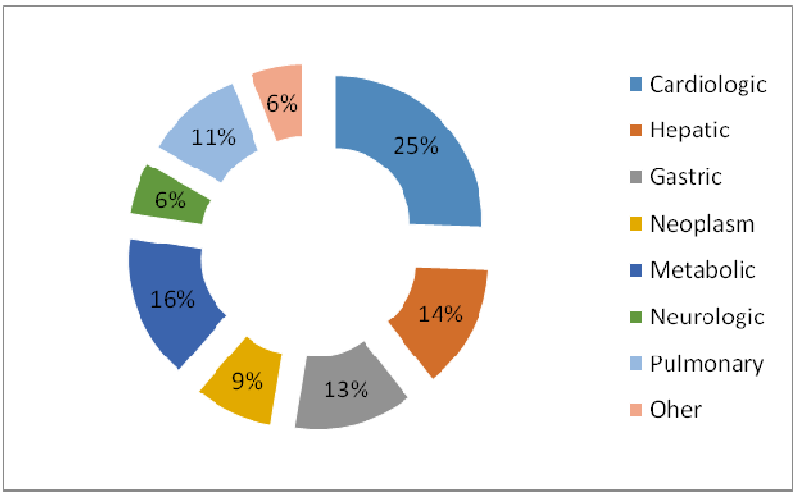
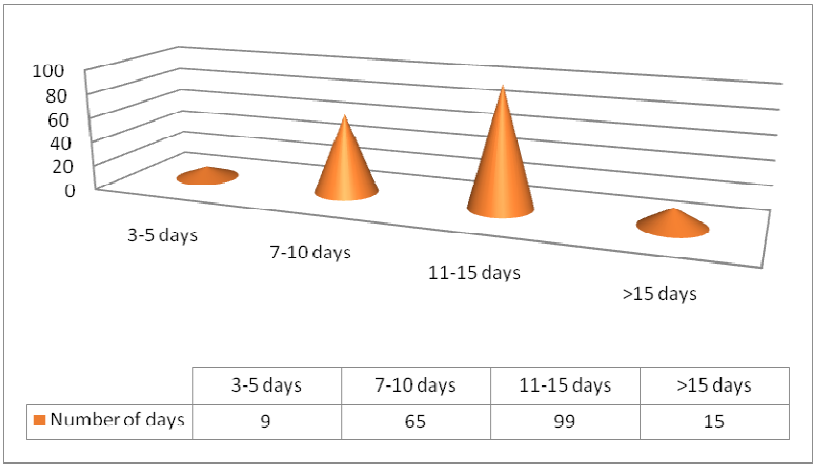


Figure 2 Comorbidity of the patients



	3-5 days	7-10 days	11-15 days	>15 days
Number of days	9	65	99	15

Figure 3 Number of days of hospitalization

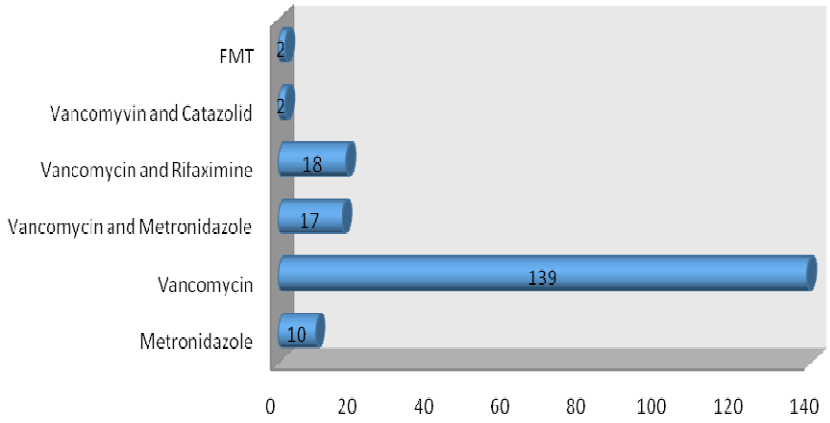
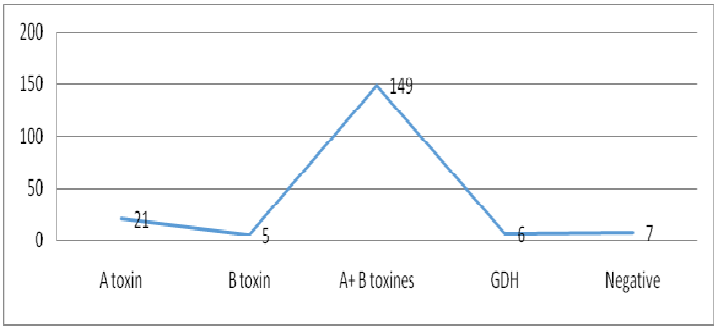


Figure 4 Treatment administrated

either oral Metronidazole (500mg every 8 hours) or Vancomycin (125mg every 6 hours) for 10–14 days (Roy et al., 2018).

In our group study, the majority of the patients received Vancomycin, followed by an association between Vancomycin and Metronidazole. In a few cases Rifaximine was administered alongside Vancomycin treatment. Cadazolid and Vancomycin was associated in 2 cases and also in 2 cases Fecalmicrobiota transplant (FMT) was performed.

A complete diagnosis of CDI requires both clinical symptoms and a positive laboratory tests. Several methods are recommended for the diagnosis of CDI, including toxicogenic culture, enzyme immunoassays (EIA) for toxins A, B, and/or glutamate dehydrogenase (GDH) etc (Zhong et al., 2018).In the group that we selected for our study, 21 cases came positive just for toxin A, in 5 cases just the toxin B was identified, in 7 cases nether of the toxin was present, 6 cases presented just the GDH and the rest of 149 had both toxins present.



Multiple recurrences of the disease and the prolonged hospitalization can create a stigma around the patients in society and even in their home. A lot of the patients required psychological support because of the depression created by this “chronic” suffering (Carmen et al., 2016).

CONCLUSIONS

Over the last 20 years there has been a substantial increase of CDI. The first recurrence of CDI causes substantial morbidity and is a major burden on health care systems.

The rate of recurrence in our hospital is at the same level as we can find in studies (30,56%). Approximately two thirds (64,89%) of the patients included in the study presented for the first recurrence of CDI, and the rest for second to sixth episode.

Every new recurrence of CDI requires more attention and careful management according to protocols. Minimizing the number of the relapses we can reduce the social, psychological and medical burden on patients and the health care system.

Medical world should start focusing in new molecule for treatment of the disease. The presence of multiple comorbidities on elderly population makes us expect to an explosion of CDI that could ultimately can become resistant to usual treatment.

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