Clostridium difficile infection characteristics in a general surgery clinic

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Abstract. *Clostridium difficile* (CD) is an anaerobic, gram-positive bacterium that can produce a spectrum of gastrointestinal diseases ranging from pseudomembranous colitis to diarrhea to toxic megacolon. The infection is even more difficult to manage as CD produces high-end spores, suggesting that this may be the cause of the dangerous recurrent disease as well as dissemination among healthy members in the community. Spores can be hosted in the digestive tract of both symptomatic and asymptomatic patients. The most relevant risk factor in the development of *Clostridium difficile* infection (CDI) seems to be the overuse of antimicrobials. Comorbidities are another risk factor that may predispose towards more serious CDI. Treatment options vary from oral antibiotics to extensive surgical interventions. The present study aimed to analyze the prevalence, severity, and management of CDIs in a general surgery department in an effort to determine the correlative elements between the infection and surgical pathology.

Introduction

Clostridium difficile is an anaerobic, gram-positive gastrointestinal bacterium that, by producing two toxins known as A and B, can cause a spectrum of diseases ranging from pseudomembranous colitis to diarrhea or even toxic megacolon. Unfortunately, it is also a bacterium that produces high-end spores (1). This may result in recurrent disease or even the dissemination of infection among healthy members of the community. *Clostridium difficile* infection (CDI) is mostly nosocomial. Yet, recently, more and more cases of community infections have been reported (20-30%) (2), but there are areas around the globe where 41% have been reported (3). The main route of transmission of this infection is fecal-oral. The spores of this bacteria can be hosted in the digestive tract of symptomatic patients, as well as that of asymptomatic patients. Unfortunately, CD spores can survive up to 5 months on surfaces, equipment or various tools (3).

The latest guidelines of the Society of Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) recommend that symptomatic and confirmed patients suffering from a CD infection be isolated in private wards with strict precautions regarding contact with other persons until the diarrheal syndrome passes completely. The staff must wear (one time use) protective equipment permanently around these patients, to wash their hands with water and soap before exiting the salon and to clean the salons that hosted these patients with chlorine-based substances (4,5). The rules do not apply, however, to asymptomatic CD carriers.

We conducted an analysis of the prevalence, severity, and management of the CD infection in a general surgery department, trying to determine the correlative elements between CD infection and surgical pathology. We aimed to ascertain how the specific measures, means of preventing and controlling of this bacterial pathology be improved.

Patients and methods

The present work was a retrospective unicentric descriptive study and took place at the General and Emergency Surgery Clinic III of the Bucharest University Emergency Hospital during 2016-2018. All necessary data were extracted from patients' electronic health records. Statistical analysis of the

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Table I. ATLAS score.

Parameter	0 points	1 point	2 points
Age (years)	<60	60-79	>80
Temperature	<37.5˚C	37.6-38.5˚C	>38.6˚C
Leukocytes (cells/mm^3)	<16,000	16,000-25,000	>25,000
Albumin (g/dl)	>3.5	2.6-3.5	<2,5
Antibiotic			
Simultaneously systemic ICD therapy (>1 day)	No		Yes
Atlas score:		No. of patients in the present study	
0 points		4	
1 point		7	
2 points		6	
3 points		4	
4 points		2	
5 points		1	

data was performed by MedCalc software (MedCalc Software, Inc.; https://www.medcalc.org).

ATLAS score is a validated evaluation system used to predict the response to the treatment, respectively, the mortality, for patients with *Clostridium difficile* infection (6). This score was also used by us in the present study (Table I).

Results

Among the 24 patients investigated, 13 were female and were 11 male. Concerning the age of the participating patients, the youngest was 44 years while the oldest was 86 years. The average age was 64.5 years. Most of our patients were between 59 and 70 years of age (Tables II and III).

The shortest time of hospitalization was one day and the longest 64 days. The average of the days of hospitalization was 19.8 days. Most patients required between 13 and 26 days of hospitalization (Table IV). Patients (12 out of 24) required care in the intensive care unit (ICU). Six patients were hospitalized previously (Table III).

Most often, the primary pathology was associated with the digestive tract, followed by cholecyst (11 and 5 cases, respectively). In the third place, there were pathologies associated with the lower limb (4 patients), followed by the abdominal wall (2 cases), pancreas and peritoneum (1 case each).

Concerning the Atlas score, the maximum value in our study was 5 points (one patient), followed by 2 other patients with a value of 4. Four patients had an ATLAS score of 0.

In what concerns associated diseases, most patients had cardiovascular comorbidities, followed by pulmonary and metabolical (diabetes mellitus). Most patients had more than one comorbidity (Table V).

Table II. Statistical data concerning the age (years) of the patients (N=24).

Parameter	Values (years)
Lowest value	44
Highest value	86
Arithmetic mean	64.5
95% CI for the mean	59.0867 to 69.9133
Median	63.5000
95% CI for the median	57.0000 to 74.2533
Variance	164.3478
Standard deviation	12.8198

Discussion

The suspicion of *Clostridium difficile* (CD) infection should be considered for each patient who develops diarrheal syndrome during hospital admission, especially if the patient has a recent history of antibiotic treatment or previous hospital admission.

Treatment of CD infections is complicated, aimed at both improving symptoms and eradicating the infection. There are multiple treatment variants: antibiotic or non-antibiotic (probiotics, fecal transplants, surgical, antibodies, photodynamic therapy). Currently, metronidazole, vancomycin, and fidaxomycin antibiotics are used, choosing one over the other depending on the severity of the infection, cost, doctor's experience, and other factors (7). In some cases, *Clostridium difficile* infection (CDI) can even result in the need for a colostomy or even total colectomy surgery (7,8).

Eze *et al* (2) published an extensive review and meta-analysis on the risk factors for CDI and recurrent CDI from published articles between 1990 and October 2016. They found that there are more than 40 associated risk factors that can be divided into 3 distinct categories: i) Pharmacological, ii) Related to host and iii) Clinical characteristics and various interventions. Among the most common risk factors are advanced age, comorbidities, antibiotics, proton-pump inhibitors (PPIs), H2 receptor antagonist (H2RA) and exposure to settings associated with health care. Previous hospitalization is an important risk factor to be taken into consideration (9). There seems to be a difference even between infections due to

Table III. Patient sex, age, hospitalization period [including days spent in the intensive care unit (ICU)] and previous hospitalization.

Patient no.	Sex	Age (years)	Hospitalization period (days)		Previous hospitalization
			Total	ICU	
1	M	53	45	0	-
2	M	44	9	0	-
3	F	63	27	1	-
4	F	44	14	1	-
5	F	86	7	0	-
6	F	77	18	0	-
7	M	59	3	0	+
8	F	74	24	2	-
9	F	64	19	0	-
10	M	66	18	1	-
11	M	57	32	1	-
12	F	85	13	0	+
13	M	58	11	0	+
14	F	77	30	1	-
15	F	46	16	0	-
16	F	54	43	1	-
17	F	58	1	0	-
18	F	66	8	0	+
19	F	84	64	3	-
20	M	64	10	0	-
21	M	56	15	1	+
22	M	75	25	0	-
23	M	81	11	1	-
24	M	57	13	0	+

Previous hospitalization: +, previously been hospitalized; -, not previously hospitalized.

Table IV. Statistical data concerning the number of hospitalization days of the patients (N=24).

Parameter	Values (days)
Lowest value	1.0000
Highest value	64.0000
Arithmetic mean	19.8333
95% CI for the mean	13.6365 to 26.0301
Median	15.5000
95% CI for the median	11.0000 to 24.2533
Variance	215.3623
Standard deviation	14.6752

the administration of antibiotics in the hospital environment compared to those administered outside the hospital. There are also differences between the potential of an antibiotic to cause a CDI. For example, clindamycin, cephalosporins, carbapenems, fluoroquinolones, and trimethoprim/sulphonamides are associated with a doubling of the risk of acquiring a CDI in a hospital environment and with an increase in 8 to 20 times for clindamycin and 3 to 5 times for cephalosporins and quinolones in the community. An insignificant risk was found in the case of retracyclines. The risk the risk increases with the extension of the administration timeof antibiotics or with association of two or more antibiotics altogether (10). Statistical significance in the case of CDI occurrence was also found for PPI and H2RA. Although statistical associations can be made, the extent of the literature, the plausibility of these findings and the multiple drugs used in these patients alongside associate comorbidities make it difficult to have a strict causal relationship between all these risk factors and CDI (2,11). On the other hand, it seems that CDI is a relevant risk factor for anastomotic leaks in patients undergoing surgery for colon or rectal cancer (12).

Comorbidities are another risk factor that may predispose individuals towards more serious CDI. Previous studies have found that gastrointestinal comorbidities (inflammatory bowel disease, cirrhosis), congestive heart disease, chronic pulmonary disease, renal failure, and malignant neoplasms are associated with higher mortality rates among patients with CDI (9).

There are few studies available concerning CDI in the surgical setting. Most of these studies have been published

Table V. Comorbidities of the patients with CDI.

	Comorbidities							
Patient no.	Oncological	Cardiovascular	Surgical	Pulmonary	Diabetes mellitus	Renal	Cirrhosis	Pancreatic
1	-	-	-	-	+	-	-	-
2	-	-	-	+	-	-	-	+
3	-	+	-	+	-	+	-	-
4	+	-	-	+	-	+	-	-
5	+	+	+	-	+	-	-	-
6	+	+	-	-	-	-	-	-
7	-	-	-	+	-	-	-	-
8	-	+	-	-	+	-	-	-
9	-	-	-	+	-	-	-	-
10	-	+	-	-	+	-	-	-
11	-	+	-	-	-	-	-	-
12	+	-	-	-	-	-	-	-
13	-	-	-	+	-	-	+	-
14	-	+	-	-	+	+	-	-
15	-	-	+	-	-	-	-	-
16	-	+	-	+	+	-	-	-
17	-	-	-	-	-	-	-	-
18	-	-	+	-	-	-	-	-
19	-	+	+	+	-	-	-	-
20	-	+	+	+	+	-	-	-
21	-	-	-	-	-	-	-	-
22	-	+	-	-	-	-	-	-
23	+	+	-	-	-	-	-	-
24	-	+	+	-	+	-	-	-

CDI, *Clostridium difficile* infection. +, suffering from the mentioned comorbidities; -, not suffering from the respective comorbidity.

recently (in the last 5 years) in more affluent regions such as North America and Western Europe (11). Thus, there is a growing need for investigating CDI worldwide, particularly in poorer countries.

Efforts have been made to develop specific antibiotic use protocols in order to decrease the incidence of CDI among surgical patients. The main focus is on reducing perioperative antibiotic use (10). There are studies that have demonstrated the effectiveness of new antibiotic policies that recommend narrower-spectrum antibiotics as well as lower doses. These studies have reported a 2- to 6-time decreased risk of CDI. The use of additional antimicrobials, broad-spectrum antibiotics, and prolonged prophylaxis increase the risk of postoperative CDI (10).

The latest available guidelines on this particular subject are from the World Society of Emergency Surgery published in 2015 and updated in 2019. It is well known that surgery, and particularly gastrointestinal surgery, may predispose patients to the development of CDIs. Some reasons for this are the widespread use of broad-spectrum antibiotics, the increasing number of surgeries on the elderly and the immuno-compromised as well as the emergence of more virulent strains of bacteria (ribotype 027) (13-15). In regards to digestive surgeries, patients with the highest risk for an ulterior CDI development are those undergoing colectomies, small-bowel resections and gastrectomies (10).

In conclusion, patients with primary pathologies related to the digestive tract are more prone to develop CDI. Most patients included in this study had an ATLAS score of 3, while the highest score calculated was 5. Thus, the infections encountered in the studied group of patients were fortunately not severe. Most patients had more than one associated disease. Protocols for decreasing perioperative antibiotic usage should be taken into consideration as antimicrobials are the most relevant risk factor in the development of CDI.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

All the authors were involved in conceiving and designing the present study. DNP, DI and RP conceived the study. MCD, OA and GR contributed to the data collection and performed the data analysis. AP, FS and AB interpreted the results and wrote the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

Not applicable as the study was retrospective and the data were completely anonymized.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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