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Research Article

Clostridium difficile Infection: Analysis of 5-Year Data in an Italian University Hospital

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Abstract

Clostridium difficile infection (CDI) is one of the most common healthcare-associated infections. It causes a variety of diseases ranging from diarrhea to megatoxic colon and also death. Over the last twenty years, the frequency and severity of this infection have globally increased and this requires the implementation of its surveillance in hospitals. In this study, were enrolled all fecal samples arriving in the microbiology laboratory of the San Giovanni di Dio and Ruggi d'Aragona university hospital from January 2019 to December 2023 to be tested for *Clostridium difficile* toxins via an enzyme immunoassay. Then, were evaluated the positive samples, the gender and age group from which they came as well as the hospital departments in which the infection was mostly found. Out of a total of 3210 total samples, 10.4% tested positive and was mostly from female and the >75 age group. The medical wards (86.2%) are the largest fraction of departments from which the majority of positive samples were received. Since the transmission of CDI is mostly nosocomial, it is important to understand that the compliance of healthcare workers is the highlight of the measures to prevent transmission and that monitoring and surveillance of this infection is essential.

Keywords: *Clostridium difficile*; Healthcare-associated infection; Hand hygiene

Introduction

Clostridium difficile infection (CDI) is a disease due to anaerobic spore-forming, toxin-producing bacterium *Clostridium difficile*. CDI is nowadays considered one of the most serious hospital-related infections (HAIs) and the leading cause of and gastroenteritis-associated deaths in United States and Europe [1,2]. The pathogenicity of *Clostridium difficile* is due to exotoxin A and exotoxin B [3] and asymptomatic diarrhea, self-limiting diarrhea, toxic megacolon and fulminant colitis can be the different clinical manifestations of the CDI [4]. Among the major risk factors there is certainly treatment with antibiotics which weaken the intestinal bacterial flora and allow this pathogen to take over [2,5] and then a long hospitalization and an advanced age (>65 years) [6]. In these elder patients, in fact, the risk of CDI increases by 5 to 10 times and is also associated with a more serious clinical course [7]. According to data from the European surveillance on *Clostridium difficile* relating to the years 2016-2017, approximately 60% of CDI cases are related to contact with the hospital environment in the 3 months preceding hospitalization [8]. Although death associated with severe Clostridium infections has increased significantly in recent years, it remains difficult to effectively objectify the relationship between CD infection and death as the presence of comorbidities constitutes a risk factor for the development of the disease [9]. In the United States, a surveillance system has been active since 2000 to monitor *Clostridium difficile* infection rates and this is considered the most common among healthcare-related infections, accounting for 15% alone [10]. The data provided by the ECDC 2016 report relating to the monitoring of *Clostridium difficile* infection in Europe inform us that cases of CDI are estimated to be 123,997 per year [11]. CDI may be associated with the length of hospital stay which must be considered in the context of the patient's clinical picture but also of public health spending [12]. Knowing and analyzing the epidemiology of *Clostridium difficile* in hospitals is essential for implementing infection prevention plans as well as evaluate and possibly improve control practices [13]. Our study aimed to analyze the percentage of CDI cases at the San Giovanni di Dio e Ruggi D'Aragona University Hospital, identify the gender or age group most correlated with the development of CDI and identifying which departments were most involved.

Materials and Methods

Diarrheal fecal samples from patients with suspected infection by CD were collected and then tested in the microbiology laboratory using an enzyme immunoassay (EIA) method. This test detects both the presence of the membrane protein glutamate dehydrogenase (GDH) and the presence of the A and B toxins. A positive test for the GDH antigen and one of the two toxins is sufficient to confirm the diagnosis of CDI. The database containing information on the total number of samples analyzed, the samples positive for toxins A, B and GDH and information regarding the departments of origin of the patients was then analyzed.

Results

From January 2019 to December 2023, 3210 fecal samples were submitted to laboratory to be tested for CD toxins by enzyme immunoassay (EIA) and 333 (10,4%) tested positive. An increase in the number of tests was observed from 597 in 2019 to 824 in 2023 which corresponded to a relative increase in positive tests. (Table 1) the percentage of positive samples in 2019 (7.7%) and 2020 (6.3%) is stable considering that the number of samples to be tested arriving in the laboratory are on average similar in these two years and therefore the relationship ratio is almost maintained. In 2021 the percentage (9.7%) begins to increase considering that the number of total samples is lower than the previous two years (Table1) (Figure 1).

	2019	2020	2021	2022	2023
Total samples (n)	597	555	534	700	824
Positive samples (n)	46	35	52	78	120
%	7,7	6,3	9,7	11,1	15,5

Table 1: Distribution of positive samples by year.

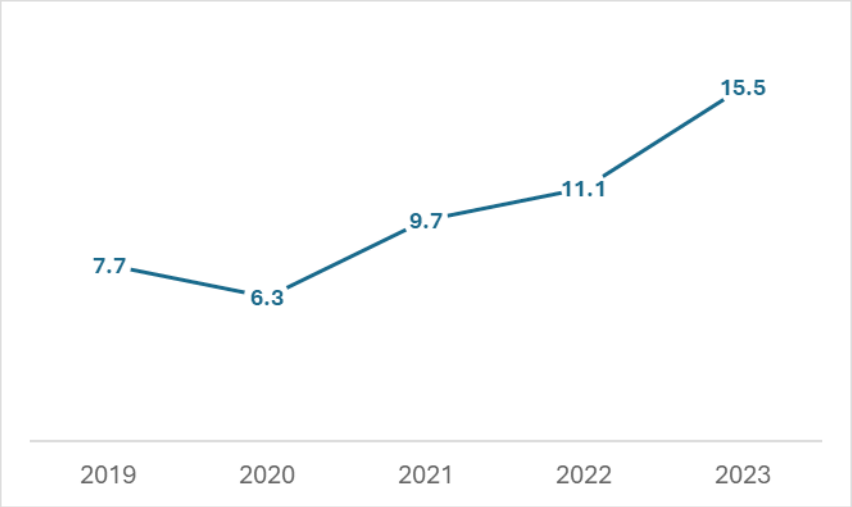

Figure 1: Distribution of the percentage of positive samples over the years.

In the following two years, the number of samples to be tested for CD increases and the percentages of positive samples also increase, 11.1% in 2022 and 15.5% in 2023. The global trend over the years shows us that the positive samples were mostly from female and the >75 age group (Table 2).

Gender	2019	2020	2021	2022	2023
	n (%)				
Male	12 (26,1%)	17 (47,2%)	24 (45,3%)	34 (43,6%)	61 (50,8%)
Female	34 (73,9%)	19 (52,8%)	29 (54,7%)	44 (56,4%)	59 (49,2%)

Table 2: Distribution among patients according to gender.

Concerning the wards, they were divided into Medical Departments, Surgery Departments and Intensive Care Departments. Among these three categories wards the medical wards (86.2%) are the largest fraction of departments from which the majority of positive samples were received, followed by the fraction of the surgical departments (8.4%) and finally by that of the intensive departments (5.4%). We also evaluated the distribution of positive samples over the years of observation in these departments and they went from 44 in 2019, 21 in 2020, 47 in 2021 and then increased to 67 in 2022 and finally to 98 in 2023 (Fig 2). Then, among the medical wards, we analyzed the data coming from the various wards to focus on the departments most involved in the production of positive samples. Figure 3 shows how the greatest number of positive samples came from Emergency medicine, Nephrology and General medicine wards, respectively with percentages of 13.6, 19.5 and 2.2 respectively.

Age Group	2019	2020	2021	2022	2023
< 60	0 (0%)	5 (13,9%)	9 (17%)	18 (23,1)	26 (21,6%)
60-75	2 (4,3%)	4 (11,1)	16 (30,2%)	15 (19,2)	35 (29,2%)
>75	44 (95,7%)	27 (75%)	28 (52,8%)	45 (57,7)	59 (49,2%)

Table 3: Distribution among patients according to age.

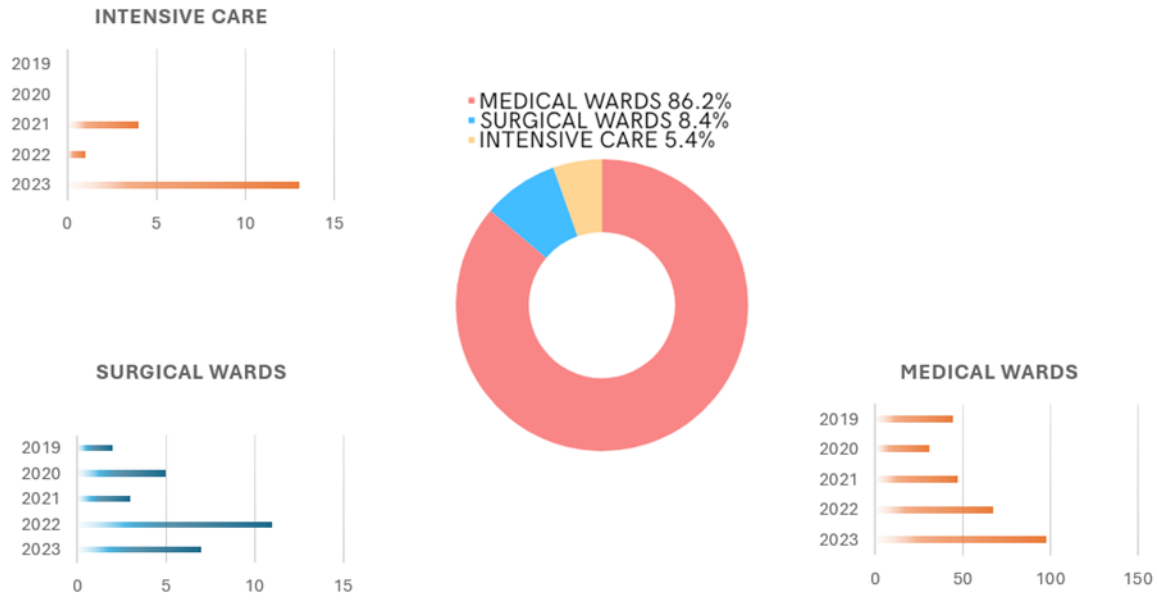

Figure 2: Distribution of positive samples in the three categories of departments analyzed and distribution for the years of observation for each individual category.

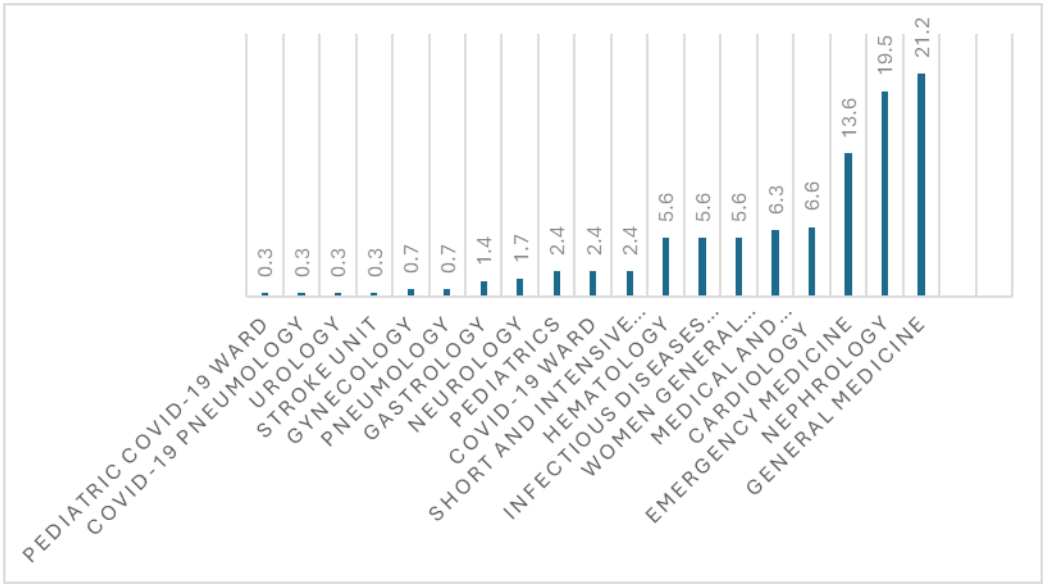

Figure 3: Distribution of positive samples by ward.

Discussion

Clostridium difficile infection is currently considered one of the major healthcare-associated infections worldwide. Due to increase in cases, need for monitoring and surveillance. In our study cohort, we were able to observe a greater increase in cases in females and in subjects aged over 77 years. Regarding gender, the data in the literature are conflicting. Several studies show how the positive samples came mostly from males. In a study conducted in Bolzano 52% of the positive samples for CD were in fact from males [14] as in the study conducted in a tertiary care academic hospital in Rome in which they were 51.7% [15]. On the other hand, in the study by Di Bella et al, 80% of the samples that tested positive for CD came from women [16]. In a health facility in northern Portugal, it was seen that women were not only more affected by CDI, but seemed to have a more severe disease than males [17]. As regards the age range, however, our data are in line with most of the literature. In fact, the patients from whom fecal samples positive for CD mostly come are on average over 60 years old. Concerning the distribution of positive cases in the departments, we were able to observe a greater distribution of cases in the medical wards compared to the surgical wards and intensive care unit. The attribution of a greater percentage of CD cases to the different wards is still controversial. Studies such as that of Hensgen et al have highlighted how patients admitted to surgical wards and intensive care units were not associated with a higher percentage of CD, while other studies such as the one by Goorhuis et al underlined that patients residing in these two ward categories had a higher rate of CD infection than other patients [18]. The greatest number of positive samples came from Emergency medicine, Nephrology and General medicine wards. In the case of nephrology patients, the increased risk of CDI can be justified by the number of infections resulting in the use of antibiotics which can in the long run cause intestinal dysbiosis [19] in the other two departments there are patients with different types of diseases which can therefore be considered comorbidities that compromise the patient's immune system which therefore becomes more susceptible to contracting a nosocomial infection. This scenario highlights how it is necessary to reiterate the importance of good prevention to stem the spread of CDI in the departments, especially in areas most at risk due to immunocompromised patients or with various comorbidities that increase the risk of contracting CDI. The hands of healthcare workers are undoubtedly the most important route of transmission of the vegetative forms as well as the spores of *Clostridium difficile*. It is absolutely necessary to keep in mind the WHO guidelines which identify the main moments in which to carry out correct hand hygiene: before and after contact with the patient, before an aseptic action, after any contact with the surfaces surrounding the patient and when comes into contact with a biological liquid or, more generally, with contaminated material [20-22]. (WHO Guidelines on Hand Hygiene in Health Care) Furthermore, environmental cleaning and control of the administration of antibiotic therapies must be implemented through the consolidation of antibiotic stewardship.

Conclusions

From the literature it can be seen that the incidence of CDI infections is increasing throughout the world. As since the most frequent cause of *Clostridium difficile* infection is nosocomial transmission. It is clear that epidemiological surveillance and control measures, especially those relating to hand hygiene of healthcare workers, take a central role into prevent and control the spread of CDI. So, in the case of *Clostridium difficile* infection, it is necessary to combine surveillance with a monitoring activity of preventive actions and in particular on educating patient care staff about cross contamination. Following prospective observational studies are desirable to analyze the future course of CDI infection and evaluate relationships of this disease with other comorbidities and with hospitalization times.

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Conflicts of Interest: The authors declare no conflicts of interest.

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