Original Research Article

A study of clostridium difficile and factors associated with it at tertiary care centre

Rashmi Chandragouda Meti[1], Anand Nagalikar[2*]

[1]Associate Professor, Department of Microbiology, Kamineni Institute of Medical Sciences, Narketpalli Telangana, INDIA.
[2]Associate Professor, Department of Pathology, ESIC Medical college Kalaburagi, Karnataka, INDIA.
Email: anagalikar@gmail.com

Abstract

Background: C. difficile is responsible for nosocomial diarrhoea in economically developed countries. Among all the risk factors involved, antibiotics are the most important risk factor along with advanced age. **Aim:** To study the Clostridium difficile and factors associated with it. **Material and Methods:** A total of 70 patients who presented to medicine outpatient department with diarrhea were studied for C. difficile toxin production and associated risk factors. Toxin detection was done by using C. Diff Quik Chek Complete® (TECHLAB, Blacksburg, VA, USA), a rapid membrane enzyme immunoassay. **Results:** Majority of the patients i.e., 31 (44.3%) were between the age group of 51-60 years followed by 18 (25.7%) 61-70 years, 11 (15.7%) 41-50 years. Out of the 70 patients 9 were found to be toxin positive. Most of the toxin-positive patients were between 51-60 years of age. Four of the nine toxin-positive cases were from ICU (44.4%) and three cases from SICU (33.3%) and two cases were from general medicine and (22.2%). All 70 cases were on multiple antibiotics which included cephalosporins 58 (82.8%) and fluoroquinolones 24 (34.3%). **Conclusion:** Elderly patients are more susceptible for toxin-positive strains of C. difficile and patients in ICU showed more toxin-positive cases, indicating the widespread usage of antibiotics in this ward.
Key Word: Clostridium difficile, toxin detection, intensive care units, antibiotics

[*]**Address for Correspondence:**
Dr. Anand Nagalikar, Associate Professor, Department of Pathology, ESIC Medical college Kalaburagi, Karnataka, INDIA.
Email: anagalikar@gmail.com
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INTRODUCTION

Clostridium difficile is a spore-forming, anaerobic, Gram-positive bacillus exists as normal flora of the gut in around 2% of healthy individuals.[1] It is responsible for nosocomial diarrhoea in economically developed countries. It is also the aetiological agent for almost all cases of pseudomembranous colitis (PMC) and 15-25% of antibiotic associated diarrhoea.[2,3] Due to the emergence of virulent strains of C. difficile, frequency and severity of C. difficile associated disease (CDAD) has been reported to be increasing in recent years. Among all the risk factors involved, antibiotics are the most important risk factor. Even though antibiotics are regarded as the primary risk factor, additional host-related and environmental factors control the severity of the disease. Severely ill patients with compromised immune function are particularly susceptible to CDAD.[4] The incidence of C. difficile infection rises with increasing age, particularly so in the elderly. Identifiable risk factors involving gastrointestinal diseases are inflammatory bowel disease, bowel ischaemia, mechanical bowel cleansing, enteric infections that change colonic microflora, prolonged presence of a nasogastric tube for enteral feeding, use of enemas, gastrointestinal stimulants and stool softeners. The present study was conducted to study the Clostridium difficile and factors associated with it.

MATERIAL AND METHODS

This prospective study was conducted in the Department of Microbiology of a tertiary care teaching hospital over a period of two years. A total of 70 patients who presented

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to medicine outpatient department with diarrhea were studied for C. difficile toxin production and associated risk factors.

Inclusion criteria

- Patients with diarrhea
- Patients with recent history of exposure to antibiotics and/or antiulcer drugs,
- All patients with inflammatory bowel disease

Exclusion criteria

- Patients with formed stools and
- Patients who had received partial or complete treatment for C. difficile infection.

Sample collection & processing: Stool samples were collected from all patients with diarrhea, i.e., watery, loose, or non-formed stools (taking the shape of the container) and having a history of antibiotic therapy or chemotherapy during the last 6 weeks or a previous diagnosis of C. difficile. The samples were collected in a clean, dry disposable container. Only freshly taken specimens were processed, and if the tests could not be performed immediately, they were kept at 4°C–8°C until processing. Stool culture was done by inoculating the samples onto Blood agar, MacConkey agar and Deoxycholate Citrate agar plates (Hi-Media, Mumbai, India) and incubating at 37°C overnight. Any non-lactose-fermenting colony was processed further by standard laboratory methods to rule out other causes of diarrhea. Stool wet mount was done for the presence of any helminthic egg or protozoa. Fecal leukocyte test (FLT) was done by methylene blue staining for the presence of white blood cells (WBC's) being noted. FLT was taken as positive if fecal leukocyte was ≥1 or ≥5 WBC/hpf.

Detection of toxins: The test was done using C. Diff Quik Chek Complete ® (TECHLAB, Blacksburg, VA, USA), a rapid membrane enzyme immunoassay for simultaneous detection of C. difficile glutamate dehydrogenase (GDH) antigen and toxins A and B using specific antibodies in a single reaction well. Using the manufacturer's instructions, the tests were performed, and the results were interpreted.

RESULTS

A total of 70 patients suspected to have *C. difficile* infection were included in this study. Of the 70 patients, 42 (60%) were male and 28 (40%) were female. Majority of the patients i.e., 31 (44.3%) were between the age group of 51-60 years followed by 18 (25.7%) 61-70 years, 11 (15.7%) 41-50 years and 7 (10%) 31-40 years and 2 (2.8%) between 71-80 years. The maximum number of suspected cases of CDI were from general medicine 38 (54.3%) followed by Medical Intensive Care Unit 24 (34.3%), Surgical Intensive Care Unit (SICU) 8 (11.4%). Out of the 70 patients 9 were found to be toxin positive. Most of the toxin-positive patients were between 51 and 60 years of age, and there was equal distribution between both the sexes. Four of the nine toxin-positive cases were from ICU (44.4%) and three cases from SICU (33.3%) and two cases were from general medicine and (22.2%). In this study, all 70 cases were on multiple antibiotics which included cephalosporins 58 (82.8%), fluoroquinolones 24 (34.3%), aminoglycosides 13 (18.6%), macrolides 6 (8.6%), metronidazole 64 (91.4%) and vancomycin 4 (5.7%). None of the toxin-positive patients were on clindamycin.

DISCUSSION

Diarrhea in hospitalized patients leads to increased length of stay and high mortality. *C. difficile* is now widely recognized cause of nosocomial diarrhea with a prevalence rate of 3% to 29%.[5-7] Most previous studies about CDI in India have shown prevalence rates ranging from 7.1% to 26.6%.[5,8] Advanced age was a well-known risk factor associated with CDI due to various factors such as increased use of antibiotics in these patients and presence of several predisposing factors such as severe underlying diseases, co-morbid conditions, and waning of immunity.[1,9,10] In our study, most of the patients were between the age group of 51-60 years, and more number of toxin-positive cases (4 of 9 cases) were from this age group, which was consistent with the study done by Vishwanath *et al.*[11] In our study, out of the nine toxin-positive cases, 5 (55.6%) were female and 4 (44.4%) were male. Chaudhry *et al.*[12] also found similar observation. Four of the nine toxin-positive cases were from ICU (44.4%) and three cases from SICU (33.3%) and two cases were from general medicine and (22.2%). Patients admitted to intensive care units are serious and antibiotics are widely used in these wards.[1,4,13] In this study, all 70 cases were on multiple antibiotics which included cephalosporins 58 (82.8%), fluoroquinolones 24 (34.3%), aminoglycosides 13 (18.6%), macrolides 6 (8.6%), metronidazole 64 (91.4%) and vancomycin 4 (5.7%). CDI was found to be frequently associated with cephalosporins, clindamycin and broad-spectrum penicillins, and quinolones.[14] The clinical practice guidelines update by the Society for Healthcare Epidemiology of America and Infectious Diseases Society of America suggest that metronidazole be the drug of choice for the initial episode of mild-to-moderate CDI, and vancomycin be used for initial episode of severe CDI.[15] In our study, metronidazole was used in 91.4% cases and 5.7% cases were treated with vancomycin.

CONCLUSION

To conclude, elderly patients are more susceptible for toxin-positive strains of C. difficile and there was no difference in gender. Patients in ICU showed more toxin-positive cases, indicating the widespread usage of antibiotics in this ward.

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