Original Article

TO DETERMINE THE FREQUENCY OF CLOSTRIDIUM DIFFICILE INFECTION IN ANTIBIOTIC ASSOCIATED DIARRHEA

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ABSTRACT

Background: Antibiotic associated diarrhea (AAD) is characterized by loose, watery stools, three or more times a day after intake of antibiotics. It is important to exclude all other possible causes of diarrhea before labeling it AAD. To determine the frequency of clostridium difficile infection in antibiotic associated diarrhea.

Material and Methods: It was a cross sectional study done in department of Gastroenterology, outpatient clinic, and ward, AIMC/ Jinnah Hospital, Lahore from 23 May 2019 to 23 November 2020. 234 patients fulfilling the selection criteria were enrolled in the study from the outpatient department and ward of Gastroenterology, Jinnah Hospital Lahore. Informed verbal consent was obtained and patients were subjected to focused history and physical examination as well as their demographic details were recorded. Antibiotics taken by the patient were documented. The antibiotic was withdrawn and the patient was treated per hospital protocol. A stool culture was sent for all patients to see CDI. The patient was labeled as CDI positive if stool culture is positive. All this information was recorded on a predesigned annexure.

Results: Out of 234 cases of antibiotic induced diarrhea; the Mean Age was 55 ±13 years (minimum was 27 and maximum was 66 years) 56% of cases were male and 44% cases were female, 28.6% of cases had age < 50 years and 71.4% cases had age ≥ 50 years, 54.7% cases used Beta-Lactam antibiotics and 45.3% cases used non- Beta-Lactam antibiotics, 68.4% cases had Bristol grade 6 and 31.6% cases had Bristol grade 7. Out of 234 cases of antibiotic associated diarrhea; 43.6% cases had CD infection and 56.4% cases had No CD infection. Stratification 0f CDI was done with regards to age groups, Gender, type of antibiotic used and Bristol grade; p-value was found to be 0.35, 0.41, 0.4 and 0.03 respectively.

Conclusion: The majority of patients with antibiotic induced diarrhea were male, had older age, used Beta-lactam antibiotics, had Bristol grade 6 and had a non-CD infection. Regarding CD infection; it was more common in older age, female gender and Beta-lactam antibiotic users; but associations were not significant. However, CD infection was more common in antibiotic induced diarrhea of Bristol grade 7 and the association was significant.

Key Words: Antibiotic, Diarrhea, Clostridium, Infection

doi: https://doi.org/10.51127/JAMDCV5I1OA06

How to cite this:
Bakr AA, Aslam N, Ghias M, Mehfooz I. To determine the frequency of clostridium difficile infection in antibiotic associated diarrhea. JAMDC. 2023;5(1): 38-42
doi: https://doi.org/10.51127/JAMDCV5I1OA06

INTRODUCTION

Antibiotic associated diarrhea (AAD) is characterized by loose, watery stools, three or more times a day after intake of antibiotics.[1] It is important to exclude all other possible causes of diarrhea before labeling it AAD. It occurs as a result of an overgrowth of some pathogenic intestinal organisms or due to a reduced concentration of fecal flora. Almost all antibiotics are implicated in the

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pathogenesis of AAD especially cephalosporins, penicillins aminoglycoside, fluoroquinolones and clindamycin. Simultaneous intake of multiple antibiotics increased duration of antibiotic treatment, history of diarrhea after antibiotics, and age of more than 65 years are important risk factors for AAD.[2,3]

Clostridium difficile (CD) is a spore-forming gram-positive anaerobic bacteria. It is normal commensal in 1-3% of normal adults. Above mentioned antibiotics may cause CD to overgrow and produce toxins A and B resulting in clostridium difficile infection (CDI). It is responsible for approximately 20% of cases of AAD. CDI causes inflammation of bowel mucosa which in turn causes diarrhea. CDI may range from simple diarrhea to life threatening condition called pseudomembranous colitis. With the increasing use of antibiotics, CDI is becoming one of the leading causes of hospitalization and deaths[1] and the severity of CDI has dramatically increased over the last decade.[2]

CDI prevalence varies worldwide and is estimated to be 0.9-2% in the general population, 1% in the European population and 3% in the Asian population.[3] In a study conducted in Iran, CDI was found to be positive in 21% of patients with diarrhea.[4] In Chinese studies, CD was isolated in 8.7%-30% of stool samples.[4,5] A study conducted in Karachi showed that CD was positive in 29.18% of AAD.[6]

The rationale for this study was that data on CDI incidence from Pakistan is scarce. Furthermore, in a country like Pakistan, there is depressed nutritional and immunological status and injudicious use of antibiotics which pose a threat of a very high prevalence of CDI. There is global emergence of resistant strains of CDI, its frequency and strains in our country would be different from the western world. So by knowing the frequency, the physician can predict the existence of the disease in a patient presenting with diarrhea after antibiotic use. So, the patients can be diagnosed at early stages by applying screening tests and definite treatment can be started to halt the disease progression. This may reduce morbidity and mortality associated with this grave but treatable disease.

MATERIAL AND METHODS

This was a cross-sectional, descriptive study that was done in OPD and ward of Gastroenterology, Jinnah Hospital Lahore. The duration of the study was 18 months from 23 May 2019 to 23 November 2020. The sample size was calculated by using the WHO calculator. The sample size came to be 234 by keeping the confidence interval at 95%, relative precision at 20%, 5% margin of error and anticipated CDI incidence at 29.18%.[7] Sampling technique was Non-probability consecutive sampling. The patient either male or female and between the ages of 16-70 years included due to any cause in the hospital who developed diarrhea after at least three days of antibiotics(even a single dose of antibiotic). There should not be a history of diarrhea in the last two weeks before starting antibiotics. Exclusion criteria involved the presence of other causes of chronic diarrhea like IBS, IBD, malabsorption syndrome, neoplasms, celiac disease, thyrotoxicosis assessed by history and clinical examination and patients with unstable cardiopulmonary, neurological, or psychiatric disease assessed by history, examination, clinical record and laboratory tests TFTs, Celiac screen and endoscopy.

Two hundred and thirty-four medical outpatients who fulfilled inclusion criteria were enrolled at Jinnah Hospital Lahore after written informed consent and subjected to focused history and physical examination as well as their demographic details were recorded. Antibiotics taken by the patient were documented. The antibiotic was withdrawn and the patient was treated per hospital protocol. A stool culture was sent for all patients to see CDI. The patient was labeled as CDI positive if stool culture is positive. All data were entered in the same proforma.

Statistical analysis was done using SPSS version 22. Frequency and percentage were

calculated for qualitative data like gender and presence of CDI. Mean + standard deviation was calculated for quantitative data like age. Data was stratified for age and gender type of antibiotics used. Post-stratification chi-square was applied to see any effect modifier by considering p value<0.05 as significant.

RESULTS

This study was conducted on 234 cases. The mean age was 55 ±13 years (minimum was 27 and maximum was 66 years). Out of 234 cases of antibiotic induced diarrhea; 56% cases were male and 44% cases were female, 28.6% cases had age < 50 years and 71.4% cases had age ≥ 50 years, 54.7% cases used Beta-Lactam antibiotics and 45.3% cases used non- Beta-Lactam antibiotics, 68.4% cases had Bristol grade 6 and 31.6% cases had Bristol grade 7. Stratification 0f CDI was done with regards to age groups, Gender, type of antibiotic used and Bristol grade; p-value was found to be 0.35, 0.41, 0.4 and 0.03 respectively.

Table-1: Distributions of the variable with frequency and percentage

Variable		Frequency	Percentage
Age group	Less than 50 years	67	28.6
	Equal or more than 50 years	167	71.4
Gender	Male	131	56
	Female	103	44
Antibiotic type	Beta Lactum	128	54.7
	Other	106	45.3
Bristol grade	06	160	68.4
	07	74	31.6
CDI	Yes	102	43.6
	No	132	56.4

Table-2: Stratification of variables with regards to CDI (n = 234)

Variable		CDI		p-value
		Yes	No	
Age group	Less than 50 years	26	41	0.35
	Equal or more than 50 years	76	91	
Gender	Male	54	77	0.41
	Female	48	55	
Antibiotic type	Beta Lactum	59	69	0.4
	Other	43	63	
Bristol score	06	62	98	0.03
	07	40	34	

DISCUSSION

Depending on the specific drug, the host's defense, and exposure to infections, AAD commonly affects 5–35% of patients taking antibiotics. The alteration of the normal microbiota, which leads to pathogen overgrowth or metabolic abnormalities, may play a role in the etiology of AAD. The first step in treating AAD is early diagnosis, which is then followed by efficient therapy and the implementation of control measures. Clostridium difficile infection (CDI) is most frequently contracted in conjunction with the use of antibiotics, which leads to the disturbance of the normal colonic microbiota. After Ingestion, C. difficile spores vegetate, grow, and exude toxins that cause CDI and in most instances, cause diarrhea and pseudomembranous colitis (PMC).

Since 2000, rates and severity of CDI significantly rose in the Western population. In 2005, Hospitals in Montreal, Quebec, reported four times higher rates than the baseline year of 1997, with mortality rising from 1.5% to 6.9%. An epidemic strain, also known as NAP1/BI/027, has been detected in North America, Europe, and Asia. This organism has the potential to produce 23 times more toxin A and toxin B as a control strain in vitro,[3] third toxin (binary toxin

CDT), and has high-level resistance to fluoroquinolones.[3] Another strain that also possesses binary toxin and is linked to high mortality in humans is toxin type V, ribotype 078 and it will continue to be implicated in outbreaks. The frequency of the NAP1/BI/027 strain in Europe has declined over the past five years.[7] However, there is no report of a decline in CDI rates or NAP1/BI/027 incidence in other parts of the world; the latter strain continues to account for 25–35% of all CDIs.

The most frequent symptom of C. difficile is diarrhea. Stools are typically watery or mucoid, soft and unformed, and have a distinct odor. They are not usually bloody. Fever, abdominal pain, and leukocytosis are the other clinical characteristics. The diagnosis of CDI is commonly missed when adynamic ileus causes a halt of stool passage. Such patients are at a higher risk of developing sepsis and toxic megacolon from C. difficile infection.[8-10]

CDI has a recurrence rate of 15%-30%. Relapse or reinfections with a different strain are both examples of recurrences. Susceptibility to recurrence is probably due to the ongoing disturbance of the fecal flora by antibiotics.[11-15] This study was conducted on 234 cases. The majority of patients with antibiotic-associated diarrhea were men, older than the average age, beta-lactam users, bristol grade 6 patients, and those with non-CD infections. Although there was a higher prevalence of CD infection among older people, women, and those who used beta-lactam antibiotics, these correlations were not statistically significant. However, there was a substantial correlation between CD infection and antibiotic-induced diarrhea in Bristol grade 7. The results of this study support our objectives. A large-scale population-based study is required for achieving significant results, which can be generalized.

CONCLUSION

Our study highlights that a considerable number of AAD cases were found to have CDI. Early detection of CDI is of paramount importance, as with appropriate measures we can reduce morbidity and mortality. The following inferences can be drawn from the study: 1. C. difficile-associated disease is a growing problem in nosocomial and community settings. 2. Most culprit drugs were found to be Beta-lactam antibiotics. 3. Clinical suspicion is more important because stool assays for diagnosing CDI are not widely available. Hospitalized patients receiving antibiotics are at greater risk of acquiring CDI. 4. Infection control procedures can offer a potential improvement in outcome and can cause a significant reduction in public health-related expenditures.

Financial disclosure: None
Conflict of interest: None

AUTHOR'S CONTRIBUTION

AAB: Concieved idea, main researcher and supervisor
NA: Data collection and data analysis
MG: Critical review
IM: Proof reading and manuscript writing

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