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Prevalence and Risk Factors of Clostridium Difficile Infection in Patients with IBD in a Tertiary Care Hospital, in South India

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Abstract: ***Background: Inflammatory Bowel Disease (IBD) patients are increasingly susceptible to Clostridium difficile infection (CDI), a critical healthcare-associated challenge characterized by complex interactions between immunological alterations, antibiotic exposure, and gut microbiome disruption. This study aims to comprehensively investigate the risk factors, clinical characteristics for CDI among IBD patients in a tertiary care hospital setting. Methods: This cross-sectional observational study was conducted over 12 months, enrolling 20 IBD patients. The study employed comprehensive diagnostic approaches including Glutamate Dehydrogenase (GDH) screening, detailed toxin typing, expanded comorbidity assessment, and thorough symptom evaluation. Stool samples underwent rigorous microbiological investigations, including rapid antigen detection, molecular testing, bacterial culture, and antibiotic susceptibility testing. Statistical analysis utilized SPSS software, with descriptive statistics, frequencies, and chi-square tests to assess variable associations. Results: The study revealed a male-predominant population (65%), with 45% aged 31-45 years. Notably, 100% of patients tested positive for GDH, with 80% positive for Toxin A and 40% for Toxin B. Comorbidities were significant, with 40% having diabetes mellitus. Symptomatology was pronounced, with 90% experiencing fever and 100% reporting abdominal pain. Symptom severity was predominantly mild (80%), with 20% classified as severe. Antibiotic usage data indicated that 30% of patients had taken Ciprofloxacin and 15% had used Metronidazole before diagnosis. Conclusion: The study provides critical insights into the CDI-IBD relationship, highlighting the need for enhanced screening protocols, targeted antimicrobial interventions, and personalized patient monitoring strategies. Future research should focus on larger, multi-center studies and detailed investigations of gender-specific risk factors.***

Keywords: Inflammatory Bowel Disease, Clostridium difficile Infection, antibiotic resistance, Antibiotics, gut microbiome, toxin typing

1. Introduction

Inflammatory Bowel Disease (IBD), comprising Crohn's disease and ulcerative colitis, is a complex group of chronic inflammatory conditions affecting the gastrointestinal tract. These conditions involve recurrent inflammation and immune dysfunction, significantly affecting patients' quality of life and long-term health [1]. The increasing global prevalence of IBD, particularly in developing countries, has drawn significant attention to understanding its associated complications and comorbidities.

Clostridium difficile infection (CDI) represents a critical and increasingly prevalent healthcare-associated challenge, especially among patients with underlying inflammatory conditions such as IBD [2]. The risk of CDI in IBD patients is multifactorial, stemming from complex interactions between disease-specific immunological alterations, frequent antibiotic exposure, and altered gut microbiome composition [3]. Immunosuppressive therapies commonly used in IBD management, including corticosteroids and biologic agents, further contribute to heightened susceptibility to opportunistic infections like CDI [4].

Recent epidemiological studies have demonstrated a disproportionately higher incidence of Clostridium difficile infection among IBD patients compared to the general population. Emerging evidence suggests that the underlying inflammatory state, coupled with frequent hospitalizations and therapeutic interventions, creates a unique microenvironment that predisposes these patients to CDI [5]. The potential consequences of CDI in IBD patients are particularly concerning, with increased risks of disease exacerbation, prolonged hospitalization, and higher mortality rates [6].

Despite substantial research, significant knowledge gaps persist regarding the precise mechanisms of CDI development in IBD patients, optimal screening strategies, and targeted prevention approaches. Understanding the intricate relationship between IBD and CDI is crucial for developing evidence-based management protocols and improving patient outcomes [7].

This study seeks to identify key risk factors, clinical manifestations for Clostridium difficile infection in IBD patients within a tertiary care hospital setting. The findings from this study provide critical insights for clinicians in optimizing treatment strategies and reducing CDI-related complications among IBD patients.

2. Methodology

Study Design and Setting: This was a cross-sectional observational study conducted at the Department of Gastroenterology in a tertiary care hospital over a 12-month period from January to December 2023. The research focused specifically on the interaction between Inflammatory Bowel Disease (IBD) and Clostridium difficile infection.

Patient Selection: A total of 20 IBD patients were prospectively enrolled, with an emphasis on comprehensive screening. The inclusion criteria were modified to prioritize:

- Age of 20 years and above
- Both outpatient and inpatient visits
- Patients with comorbidities
- Those with potential risk factors including alcohol and smoking history

Diagnostic approach: The diagnostic methodology was enhanced to include:

- Comprehensive GDH screening (100% positive in the study)
- Detailed toxin typing (Toxin A and B detection)
- Expanded comorbidity assessment
- Thorough symptom evaluation, with particular attention to:
  - Abdominal pain (100% occurrence)
  - Fever (90% occurrence)
  - Diarrhea duration assessment

Microbiological Investigations: While maintaining the original methods, special focus was placed on:

- Glutamate Dehydrogenase (GDH) screening
- Comprehensive toxin typing
- Correlation of antibiotic usage with infection status

Laboratory Procedures: Stool samples were collected under sterile conditions and transported to the microbiology laboratory within two hours of collection. Each sample underwent:

- Initial screening with rapid antigen detection tests
- Confirmatory molecular testing
- Bacterial culture on selective media
- Antibiotic susceptibility testing for identified C. difficile isolates

Clinical Assessment: Participants were monitored for:

- Presence of C. difficile infection
- Symptoms of CDI (diarrhea, abdominal pain, fever)
- Requirement for additional medical interventions

Statistical Analysis: Data were analyzed using SPSS software (version 26.0). Descriptive statistics were used to summarize patient characteristics. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. Chi-square test and Fisher's exact test were employed to assess associations between variables. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: Written informed consent was obtained from all participants prior to study enrollment. Confidentiality of patient information was maintained throughout the study. Participants were free to withdraw from the study at any point without any consequences to their medical care.

3. Results

The demographic analysis reveals a male-predominant population (65%), with 45% aged between 31 and 45 years. The diarrhea duration shows that most patients (45%) experienced symptoms for 6-10 days. Notably, 100% of patients tested positive for GDH (Glutamate Dehydrogenase), indicating widespread C. difficile presence. Toxin typing showed 80% positive for Toxin A and 40% for Toxin B. Comorbidities were significant, with 40% of patients having diabetes mellitus and 30% having both alcohol and smoking history. Symptomatology was striking, with 90% experiencing fever and 100% reporting abdominal pain. Symptom severity was predominantly mild (80%), with 20% classified as severe.

Table 1: Demographic and Clinical Characteristics

		Frequency	Percentage
Age	18-30 years	5	25%
	31-45 years	9	45%
	46-60 years	6	30%
Gender	Males	13	65%
	Females	7	35%
Diarrhoea duration	<5 days	7	35%
	6 to 10 days	9	45%
	11 to 15 days	3	15%
	>15 days	1	5%
GDH	Positive	20	100%
Toxin Type	Toxin A	16	80%
	Toxin B	8	40%
Co-morbidties	DM	8	40%
	Hypertension	1	5%
	CVA	1	5%
	PPI	1	5%
	Alcohol	5	25%
	Alcohol/smoking	6	30%
Symptoms	Fever	18	90%
	Abdominal pain	20	100%
Symptom Severity	Mild	16	80%
	Moderate	0	0%
	Severe	4	20%

The antibiotic usage data showed that 25% of patients had antibiotic exposure 6-10 days prior to diagnosis, with 30% having used Ciprofloxacin and 15% using Metronidazole. Notably, 70% of patients had no recent antibiotic use recorded.

Table 2: Antibiotic Usage

		Frequency	Percentage
Antibiotic days prior to diagnosis	<5 days	3	15%
	6 to 10 days	5	25%
	>10 days	1	5%
	NA	14	70%
Antibiotic used	Ciprofloxacin	6	30%
	Metronidazole	3	15%

The Mayo score distribution indicates that most patients (55%) were at Mayo 2 level, suggesting moderate disease activity. Only 5% showed pseudomembrane formation, which is relatively low compared to the total patient population.

Table 3: Disease Severity

		Frequency	Percentage
Mayo score	Mayo 1	6	30%
	Mayo 2	11	55%
	Mayo 3	3	15%
Pseudomembrane	Yes	1	5%
	Nil	19	95%

4. Discussion

Our study provides critical insights into the complex relationship between Clostridium difficile infection (CDI) and Inflammatory Bowel Disease (IBD) in a tertiary care hospital setting. The findings highlight several significant epidemiological and clinical characteristics that warrant detailed examination and comparison with existing literature.

Demographic and Infection Prevalence:
The study revealed a male predominance (65%) with a mean age range of 31-45 years. Many Indian literatures have shown a male predominance in the development of CDI. [8-10] This gender disparity in CDI prevalence among IBD patients is noteworthy, suggesting potential immunological or behavioral factors that may influence infection susceptibility. Comparable studies have shown varying gender distributions, indicating the need for further investigation into gender-specific risk factors.

Toxin Characteristics:
Our findings demonstrated a high prevalence of toxin detection, with 80% positive for Toxin A and 40% for Toxin B. This toxin profile differs from some previous studies. Samra Z et al. [11] reported lower toxin detection rates, suggesting potential regional or population-specific variations in C. difficile strains. The high toxin prevalence in our study underscores the significant infectious burden in IBD patients.

Symptom Characterization:
Consistent with Issa et al.'s findings, our study revealed high rates of CDI-related symptoms. Notably, 90% of patients experienced fever, and 100% reported abdominal pain. The symptom severity was predominantly mild (80%), with only 20% experiencing severe symptoms, which differs slightly from the more severe outcomes reported by Issa et al.[12]

Antibiotic Usage:
Our analysis showed 30% of patients had used Ciprofloxacin, and 15% used Metronidazole prior to diagnosis. This pattern of antibiotic use is consistent with findings by Duan R et al. [13], which highlighted the potential role of antibiotic exposure in CDI development among IBD patients. In the literature review done by Ghia et al., 22 articles showed that all the people developed CDI who were on prior antibiotics.[8]

Clinical Implications:
The study's findings have significant clinical implications. The high prevalence of CDI among IBD patients, coupled with the complex symptom profile and toxin characteristics, suggests the need for:
1) Enhanced screening protocols
2) Targeted antimicrobial interventions
3) Comprehensive comorbidity management
4) Personalized patient monitoring strategies

Limitations and Future Directions:
While our study provides valuable insights, several limitations must be acknowledged:
- Small sample size (20 patients)
- Single-center design
- Potential selection bias
- Limited generalizability

Future research should focus on:
- Larger, multi-center studies
- Detailed investigation of gender-specific risk factors
- Long-term follow-up of CDI impact on IBD progression
- Comprehensive analysis of emerging C. difficile strains

5. Conclusion

This study highlights the significant burden of CDI among IBD patients, emphasizing the need for proactive targeted screening and tailored treatment strategies. Future research should focus on larger, multi-center studies to validate these findings and explore additional risk factors affecting patient outcomes

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