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Role of Peritoneal Fluid Culture and Sensitivity for appropriate Antibiotic Therapy in Perforative Peritonitis

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Perforative peritonitis, Peritoneal fluid culture, Antibiotic susceptibility testing, India

ABSTRACT:

Background: Perforative peritonitis is a severe, life-threatening condition resulting from gastrointestinal perforations, leading to bacterial contamination of the peritoneal cavity. Early and targeted antibiotic therapy, guided by knowledge of local bacterial profiles and resistance patterns, is essential for improving clinical outcomes in affected patients. Objectives: To determine the bacterial pattern of peritoneal fluid based on culture; and to ascertain the antibacterial susceptibility of the isolated organisms. Methods: This was a hospital based analytical cross-sectional study conducted in the Department of Emergency Medicine and inpatient wards of the Government Thiruvarur Medical College and Hospital, Thiruvarur, Tamil Nadu, India between May 2021 and May 2022. Results: The study analysed 60 patients with a mean age of 49.4 years, predominantly male (90%). The duration of symptoms varied, with 18.3% presenting with symptoms lasting ≤1 day, 70% for 2-3 days, and 11.7% for over 4 days. Notably, 70% had no comorbidities. The most common site of perforation was the duodenum (50%), followed by the gastric region (40%). Surgical interventions included omental patch closure (83.3%), with a 95% survival rate; 80.7% of survivors recovered within 10 days. Peritoneal fluid cultures revealed 6.7% with no bacterial growth. Klebsiella was the most common organism isolated (40%), followed by E. coli (33.3%). Mixed cultures were found in 11.7%, with Proteus and Pseudomonas isolated less frequently. Organism distribution varied by perforation site; for instance, in gastric perforations, Klebsiella was found in 41.7% of cases, while E. coli and Klebsiella each accounted for 40.7% in duodenal perforations. Antibiotic sensitivity testing showed that 96.7% of isolates were susceptible to ciprofloxacin, with 78.3% sensitivity to ceftriaxone and amikacin. Sensitivity to ampicillin and cotrimoxazole was lower at 48.3%. Conclusion: This study highlights critical demographic, clinical, and microbiological aspects of patients with gastrointestinal perforations.

Introduction

Peritonitis remains one of the most common challenges faced by general surgeons. It continues to be a major cause of morbidity and mortality, whether it results from a simple duodenal perforation, traumatic perforation, appendicular perforation, or acute pancreatitis complicated by a pancreatic abscess.(1) Although the use of antibiotics and surgical intervention in the treatment of peritonitis has seen significant improvements in recent decades, intra-abdominal infections still present considerable challenges for surgeons.(2) Most cases of peritonitis encountered are secondary, arising from perforations in hollow viscera. Surgeons are acutely aware of the severe and potentially fatal complications associated with this condition, which can range from minor wound infections to life-threatening septic shock or systemic inflammatory response syndrome (SIRS).(3)

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Several factors complicate the treatment of peritonitis. These include the patient's age, the time interval between the onset of symptoms and presentation, the general condition and nutritional status of the patient, the presence of malignancy, and postoperative complications.(4) Additionally, the peritoneal cavity is often heavily contaminated with lethal strains of Enterobacteriaceae, including Enterococci, Escherichia coli, Klebsiella, and Proteus. These organisms can either directly trigger SIRS or produce toxins that contribute to its development.(5) In the 1930s, Altemeier isolated various microorganisms from peritoneal fluid and demonstrated their pathogenic role in intra-abdominal sepsis.(6)

Over the past three decades, antibiotic therapy for intra-abdominal infections has evolved, now grounded in robust experimental and Class 1 clinical data. Weinstein et al. were among the first to demonstrate that combination therapy targeting both aerobic and anaerobic organisms improved survival rates and reduced the formation of abscesses.(7) Current treatment strategies for peritonitis focus on addressing the underlying cause, controlling infection with systemic antibiotics, and providing supportive care to prevent the progression of SIRS. It has been observed that antibiotic therapy targeting aerobic bacteria reduces mortality but is associated with increased abscess formation, whereas treatment aimed at anaerobic bacteria results in lower abscess formation but does not significantly impact mortality.(8) As a result, combination therapy is now considered the most effective approach. A broad-spectrum antibiotic regimen, typically covering gram-positive, gram-negative, and anaerobic bacteria, is often initiated to ensure prompt treatment. However, the growing issue of antibiotic resistance poses a significant challenge to treatment outcomes. Against this background, this study analysed the various organisms found in the peritoneal fluid cultures of patients presenting with perforative peritonitis, along with their patterns of antibiotic sensitivity and resistance.

The aim of the present study was to facilitate early and appropriate antibiotic therapy in patients with perforative peritonitis, thereby improving clinical outcomes. The objectives were to determine the bacterial pattern of peritoneal fluid based on culture; and to ascertain the antibacterial susceptibility of the isolated organisms.

Materials and Methods

This was a hospital based analytical cross-sectional study conducted in the Department of Emergency Medicine and inpatient wards of the Government Thiruvarur Medical College and Hospital, Thiruvarur, Tamil Nadu, India between May 2021 and May 2022. The study was approved by the Institutional Human Ethics Committee (IHEC). The participants were given the Participant Information Sheet (PIS) in their native language, and its contents were verbally explained to ensure their understanding and satisfaction. Enrolment into the study proceeded upon receipt of written informed consent. All the patients admitted to the Government Thiruvarur Medical College and Hospital with perforative peritonitis were included. However, patients less than 12 years of age were excluded from the present study. The minimum required sample size was estimated to be 60.

We used a purpose predesigned, semi structured, and pretested questionnaire to document the patients' sociodemographic characteristics (including age, gender), detailed clinical history (including comorbidities), findings of general physical examination, systemic examination, chest X-ray, and abdominal X-ray (in erect position). The presence of air under the diaphragm was suggestive of perforative peritonitis. Additionally, the laboratory investigations of the patients including complete blood count, blood urea, blood glucose, serum creatinine, serum electrolytes, and electrocardiogram were performed and noted. Upon confirmatory diagnosis, the patients were taken up for emergency laparotomy and perforation closure.

Surgical procedure: The patients were resuscitated, and vitals stabilised by administering intravenous fluids. Once the patient was stable, consent for the scheduled emergency laparotomy was obtained from both the patient and their attendants. In non-traumatic cases, an emergency laparotomy was performed through a midline incision. During the procedure, peritoneal fluid was collected and sent for aerobic microbiological culture. The perforation was closed with vicryl sutures, and the abdomen was closed with a drainage tube placed in situ to manage postoperative fluid accumulation. After surgery, the patient received standard postoperative care, including intravenous fluids and antibiotics. The peritoneal fluid culture results were reviewed, and antimicrobial sensitivity

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testing was conducted on the isolated organisms using the Kirby-Bauer disc diffusion method, with antibiotics such as ampicillin, amikacin, ciprofloxacin, ceftriaxone, and cotrimoxazole. The patient's antibiotic treatment was adjusted based on the culture and sensitivity results to target the specific organisms identified.

Statistical analysis: The data obtained was manually entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) v23. All the categorical variables were summarised using frequencies and percentages. Continuous variables were summarized using mean (standard deviation) and/or median (interquartile range) (based on the results of data normality, tested using Kolmogorov–Smirnov test and the Shapiro–Wilk test). To test for statistical significance, Chi square test or Fisher exact test (for categorical variables) and independent "t" test or Mann Whitney U test (for continuous variables) was used. Statistical significance was considered at p value less than 0.05.

Results

Among the 60 patients studied, the age distribution was as follows: 5% were less than 30 years old, 20% were aged 31 to 40 years, 35% were aged 41 to 50 years, 16.7% were aged 51 to 60 years, and 23.3% were over 60 years of age. The mean age of presentation was 49.4 years. The majority of participants were male (90%), while 10% were female. Regarding the duration of symptoms, 18.3% of patients presented with symptoms lasting less than or equal to 1 day, 70% had symptoms for 2 to 3 days, and 11.7% had symptoms lasting 4 days or more. Comorbidities were absent in 70% of the patients, whereas 30% had existing comorbid conditions. The most common site of perforation was the duodenum (50%), followed by the gastric region (40%), ileum (5%), jejunum (1.7%), caecum (1.7%), and sigmoid colon (1.7%). Surgical procedures performed included omental patch closure in 83.3% of cases, omental patch closure with feeding jejunostomy in 6.7%, primary closure in 6.7%, and distal gastrectomy in 3.3%. Postoperative outcomes showed a 95% survival rate, with 5% mortality. Among the 57 survivors, 80.7% recovered within 10 days or less, while 19.3% required more than 10 days for recovery.

Among the 60 patients, the peritoneal fluid culture results showed that 6.7% had no bacterial growth. The most commonly isolated organism was Klebsiella, found in 40% of cases, followed by E. coli in 33.3%. Mixed cultures of E. coli and Klebsiella were identified in 11.7% of patients. Less frequently isolated organisms included Proteus in 5% and Pseudomonas in 3.3% of cases. The distribution of cultured organisms varied according to the site of perforation. Among the 24 patients with gastric perforations, Klebsiella was the most frequently isolated organism, found in 41.7% of cases, followed by E. coli in 33.3%, E. coli and Klebsiella mixed cultures in 16.7%, and Proteus and Pseudomonas, each in 4.2%. In the 27 patients with duodenal perforations, E. coli and Klebsiella were each isolated in 40.7% of cases, followed by E. coli and Klebsiella mixed cultures in 7.4%, Proteus in 7.4%, and Pseudomonas in 3.7%. For the single jejunal perforation case, Klebsiella was isolated (100%). Among the three patients with ileal perforations, E. coli was found in 66.7% of cases, and Klebsiella was found in 33.3%. Both caecal and sigmoid perforations were singular cases; Klebsiella was isolated in the caecal perforation (100%), and a mixed culture of E. coli and Klebsiella was found in the sigmoid perforation (100%).

Among the 60 patients, antibiotic sensitivity testing revealed that the highest sensitivity was observed with ciprofloxacin, to which 96.7% of the isolates were susceptible. Sensitivity to both ceftriaxone and amikacin was found in 78.3% of cases. Ampicillin and CTZ (cotrimoxazole) showed lower sensitivity, with 48.3% of the isolates being susceptible to each of these antibiotics.

Discussion

The present study aimed to improve early and appropriate antibiotic therapy in patients with perforative peritonitis by identifying the bacterial pattern of peritoneal fluid and determining antibacterial susceptibility. In this study, the majority of patients with perforative peritonitis were male (90%), with a mean age of 49.4 years. This aligns with other studies showing a higher incidence of perforative peritonitis among males, likely due to higher exposure to risk factors such as smoking, alcohol consumption, and nonsteroidal anti-inflammatory drug (NSAID) use, which are more

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prevalent in men (Egwuonwu et al., 2019; Neupane et al., 2022).(9, 10) The age distribution reflects that the condition predominantly affects middle-aged to older individuals, which is consistent with other research suggesting that the risk of gastrointestinal perforations increases with age due to decreased tissue resilience and increased comorbidities (Yuan et al., 2023).(11) The majority of patients presented with symptoms lasting 2 to 3 days (70%), suggesting that delayed presentation is common among patients with perforative peritonitis (Al Saeed et al., 2022).(12) This delay could be due to a lack of awareness about the severity of symptoms, delayed access to healthcare facilities, or misinterpretation of early symptoms as less severe gastrointestinal disturbances. Early identification and intervention are critical, as delayed presentation is associated with increased morbidity and mortality due to the rapid progression of sepsis and systemic inflammatory response syndrome (SIRS) (Clements et al., 2021; Loganathan, 2015).(13, 14) Comorbidities were present in 30% of patients, with the remaining 70% having no existing health conditions. The presence of comorbidities, such as diabetes mellitus, hypertension, and chronic kidney disease, has been shown to adversely affect outcomes in patients with gastrointestinal perforations, as these conditions can impair wound healing, immune response, and overall physiological resilience (Al Bisher et al., 2023; Špička et al., 2022).(15, 16)

The most common site of perforation in this study was the duodenum (50%), followed by the gastric region (40%). These findings are consistent with the literature, which identifies the duodenum and stomach as the most frequent locations for perforations, often linked to peptic ulcer disease (Weledji, 2020).(17) The high incidence of duodenal and gastric perforations can be attributed to factors such as Helicobacter pylori infection, NSAID use, and other underlying gastrointestinal pathologies (Chung & Shelat, 2017; Søreide et al., 2015).(18, 19) Surgical intervention is the cornerstone of management for perforative peritonitis (van Ruler & Boermeester, 2017),(20) with omental patch closure being the most commonly performed procedure in this study (83.3%). This technique is widely used for repairing small perforations in the duodenum or stomach and has been associated with favourable outcomes (Allart et al., 2018).(21) More complex procedures, such as omental patch closure with feeding jejunostomy (6.7%), primary closure (6.7%), and distal gastrectomy (3.3%), were performed based on the location, size, and severity of the perforation.

The study's overall survival rate of 95% is commendable, reflecting effective surgical management and postoperative care. However, the 5% mortality rate, though low, underscores the severity of the condition and the potential for rapid clinical deterioration in these patients. Studies have shown that factors contributing to mortality in perforative peritonitis include advanced age, delayed presentation, and the presence of comorbidities, which can exacerbate the systemic effects of peritonitis and sepsis (Launey et al., 2017; Neupane et al., 2022).(9, 22) Among the survivors, 80.7% recovered within 10 days or less, while 19.3% required a longer recovery period. Prolonged recovery is often associated with complications such as surgical site infections, persistent sepsis, or delayed return of gastrointestinal function, which can prolong hospital stay and necessitate additional medical or surgical interventions (Ordoñez & Puyana, 2006).(23)

In this study, the most frequently isolated organisms from peritoneal fluid were Klebsiella (40%) and E. coli (33.3%), with mixed cultures of both organisms found in 11.7% of patients. This bacterial distribution is consistent with the broader literature, which identifies E. coli and Klebsiella as predominant pathogens in intra-abdominal infections, including peritonitis (Sudhaharan et al., 2018).(24) These organisms are common gut flora, and their presence in the peritoneal cavity often results from gastrointestinal perforations that breach mucosal barriers, allowing bacteria to enter the sterile peritoneal space (Sartelli et al., 2012; Sartelli et al., 2016).(25, 26) The presence of mixed cultures in 11.7% of patients emphasizes the polymicrobial nature of peritoneal infections (Shah et al., 2016),(27) which can complicate clinical management due to the varied antibiotic susceptibility profiles of different bacteria. Mixed infections may also increase the severity of the condition, as interactions between different bacterial species can enhance pathogenicity and resistance mechanisms (Martínez & Baquero, 2002).(28) Less commonly isolated organisms in this study included Proteus (5%) and Pseudomonas (3.3%), which are also known to cause secondary peritonitis, particularly in patients with underlying comorbidities or prolonged hospital

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stays (Mishra et al., 2014).(29) Pseudomonas, in particular, is associated with more severe infections and higher antibiotic resistance, which can complicate treatment outcomes (Siva et al., 2009).(30)

The distribution of bacterial isolates varied according to the site of perforation. In patients with gastric perforations, Klebsiella was the predominant organism (41.7%), followed by E. coli (33.3%). This finding suggests that gastric perforations, often linked to ulcer disease or malignancy, may favour colonization by Klebsiella, which is associated with high virulence factors such as mucoviscosity and the ability to form biofilms, enhancing its survival in adverse environments (Guerra et al., 2022).(31) For duodenal perforations, E. coli and Klebsiella were each isolated in 40.7% of cases, reflecting a similar pathogenic pattern as seen in gastric perforations. The high prevalence of E. coli in duodenal perforations may be attributed to its predominance in the upper gastrointestinal tract, where it is frequently implicated in perforations resulting from peptic ulcer disease. Interestingly, in the less common jejunal, ileal, caecal, and sigmoid perforations, Klebsiella was frequently isolated, indicating its adaptability across different sites of the gastrointestinal tract. These findings align with previous research demonstrating that Klebsiella is not limited to the upper GI tract and can cause infections in various intestinal locations due to its diverse virulence factors (Sartelli et al., 2016).(26)

Antibiotic susceptibility testing revealed that the highest sensitivity among isolates was observed with ciprofloxacin, to which 96.7% of the isolates were susceptible. This high sensitivity rate underscores ciprofloxacin's effectiveness as a broad-spectrum antibiotic commonly used in the treatment of intra-abdominal infections (Gray & Loshak, 2019).(32) Ciprofloxacin's potent bactericidal activity against Gram-negative bacteria, such as E. coli and Klebsiella, makes it a valuable choice, particularly when empirical therapy is initiated before culture results are available. Sensitivity to ceftriaxone and amikacin was observed in 78.3% of cases. These antibiotics are often employed in combination to provide synergistic effects against a broad range of Gram-negative pathogens. Ceftriaxone, a third-generation cephalosporin, offers robust coverage against Enterobacteriaceae, while amikacin is an aminoglycoside effective against resistant strains. However, the slightly lower susceptibility rates suggest that resistance to these antibiotics is an emerging concern, likely due to the overuse or misuse of these agents in clinical settings. Ampicillin and cotrimoxazole exhibited the lowest sensitivity rates, with only 48.3% of the isolates susceptible. The declining effectiveness of these antibiotics can be attributed to the widespread resistance mechanisms such as beta-lactamase production in Klebsiella and E. coli, which degrade ampicillin, and folate pathway alterations that reduce the efficacy of cotrimoxazole (Livermore, 2012).(33) The lower sensitivity rates highlight the limitations of these antibiotics in the empirical treatment of peritoneal infections, underscoring the need for routine susceptibility testing to guide therapy (Sartelli et al., 2012).(25)

Conclusion

The present study provides critical insights into the bacterial profile and antibiotic susceptibility patterns in patients with perforative peritonitis, emphasizing the significance of early and targeted antimicrobial therapy to improve clinical outcomes. The findings revealed that Klebsiella and E. coli were the most frequently isolated organisms in peritoneal fluid, with a notable presence of mixed infections that underline the polymicrobial nature of perforative peritonitis. The high sensitivity of these isolates to ciprofloxacin suggests its effectiveness as an initial empirical therapy; however, the emergence of antibiotic resistance, particularly against commonly used agents like ampicillin and cotrimoxazole, underscores the necessity for routine culture and sensitivity testing to guide appropriate antibiotic selection.

Additionally, the variation in bacterial distribution according to the site of perforation highlights the need for tailored treatment strategies based on anatomical location. The study's findings support the crucial role of timely surgical intervention combined with evidence-based antibiotic therapy to enhance patient recovery and reduce mortality. Overall, the results reinforce the importance of antimicrobial stewardship and highlight the need for ongoing surveillance of bacterial resistance patterns to optimize treatment protocols and improve outcomes for patients with perforative peritonitis.

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Table 1: Characteristics of patients with perforative peritonitis and its postoperative outcomes

		Number (N=60) (n)	Percentage (%)
Age (in years)	Less than 30	3	5.0
	31 to 40	12	20.0
	41 to 50	21	35.0
	51 to 60	10	16.7
	More than 60	14	23.3
Gender	Male	54	90.0
	Female	6	10.0
Duration of symptoms (in days)	Less than or equal to 1	11	18.3
	2 to 3	42	70.0
	More than or equal to 4	7	11.7
Comorbidity	Absent	42	70.0
	Present	18	30.0
Site of perforation	Gastric	24	40.0
	Duodenum	30	50.0
	Jejunum	1	1.7
	Ileum	3	5.0

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	Caecum	1	1.7
	Sigmoid	1	1.7
Procedure done	Omental patch closure	50	83.3
	Omental patch closure with feeding jejunostomy	4	6.7
	Primary closure	4	6.7
	Distal gastrectomy	2	3.3
Postoperative outcome	Death	3	5.0
	Survived	57	95.0
Postoperative recovery (in days) (N=57)	Less than or equal to 10	46	80.7
	More than 10	11	19.3

Table 2: Peritoneal fluid culture results

		Number (N=60) (n)	Percentage (%)
Culture organism	No growth	4	6.7
	E. Coli	20	33.3
	Klebsiella	24	40.0
	Proteus	3	5.0
	Pseudomonas	2	3.3
	E. Coli + Klebsiella	7	11.7

Table 3: Distribution of cultured organisms, by site of perforation

		Site of perforation					
		Gastric N = 24	Duodenum N = 27	Jejunum N = 1	Ileum N = 3	Caecum N = 1	Sigmoid N = 1
Culture organism	E. Coli	8 (33.3)	11 (40.7)	0 (0.0)	2 (66.7)	0 (0.0)	0 (0.0)
	Klebsiella	10 (41.7)	11 (40.7)	1 (100)	1 (33.3)	1 (100)	0 (0.0)
	Proteus	1 (4.2)	2 (7.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Pseudomonas	1 (4.2)	1 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	E. Coli + Klebsiella	4 (16.7)	2 (7.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)

Table 4: Antibiotic susceptibility testing

		Number (N=60) (n)	Percentage (%)
Sensitivity to antibiotics	Ciprofloxacin	58	96.7
	Ceftriaxone	47	78.3
	Amikacin	47	78.3
	Ampicillin	29	48.3
	CTZ	29	48.3