

Comparison of Microbiological Profile of Drained Intra-Abdominal Abscess in Patients with Crohn's Disease and Colonic Diverticulitis

✉ Reem F. Al-Rubaie*, ✉ Hayder Alqaishi*, ✉ Alaa El-Hussuna*

Aalborg University Hospital, Department of Surgery, Aalborg, Denmark

* Open Source Research Collaboration (OSRC.Network)

ABSTRACT

Aim: To investigate the microbiological profile of intra-abdominal abscesses drained from patients with Crohn's disease (CD) compared to patients with complicated diverticulitis coli (cDC).

Method: This was a retrospective, cohort, pilot study. Inclusion criteria were adult patients who underwent percutaneous ultrasonographic/computed tomography (CT) guided drainage or aspiration of abscess. Cultures were performed for all patients and tested with Gram staining. Demographic data, pre-operative medications taken for CD, abscess size, antibiotic coverage after drainage, abscess recurrence, surgical resection, resection type and post-operative complications were investigated.

Results: A total 44 patients with CD (n=18) and cDC (n=26) were investigated in this pilot study. Cultures showed mostly mixed Gram-positive and negative bacteria in both CD and cDC, but Gram-negative culture was more prevalent in cDC ($p=0.029$). The most common bacteria was *Escherichia coli* in both groups. Anaerobic bacteria were the second most common flora in patients with cDC, while *Streptococcus*, *Enterococcus*, Extended spectrum Beta Lactamase-producing organisms, *Pseudomonas*, *Morganella* and *Proteus* were the second most common in patients with CD.

Conclusion: Mixed Gram-positive and negative bacteria with *Escherichia coli* were the most common bacteria in CD and cDC. Both groups also showed significant growth of *Enterococci*, *Streptococci*, and anaerobic bacteria in culture. *Klebsiella pneumoniae* was significantly more prevalent in patients with CD.

Keywords: Crohn's disease, diverticulitis, abscess, percutaneous drainage, bacteria

Introduction

Patients with Crohn's disease (CD) may develop intra-abdominal abscesses, which occur in 10% to 28% of patients.¹ At least 80% of abscesses contain multiple bacteria types, which are typically a mixture of aerobic and anaerobic flora. The most common aerobes are *Escherichia coli* and *Enterococcus* spp., and the most common anaerobes are *Bacteroides fragilis* and *Peptostreptococcus* species. Importantly, fungal infections including *Candida albicans* may be present in chronic abscesses, especially when patients are immune-suppressed, malnourished, or on protracted courses of antibiotic therapy.^{1,2}

A recent study found bacterial isolates from CD-associated abscesses included *E. coli* (54%), *Bacteroides fragilis* (44%),

Enterococci (41%), and *Viridans streptococci* (31%).³ However, other studies also show an alarming increase in quinolone-resistant *E. coli*⁴ intrinsic third-generation cephalosporin resistant *Enterococcus faecium*⁵ and *Candida* spp.⁶ Owing to a lack of prospective studies, current treatment concepts are based on retrospective data and case series, and favor a combination of broad-spectrum antibiotic therapy and percutaneous drainage, followed by delayed surgical therapy if necessary.^{7,8}

Abscesses may also complicate up to 30% of cases with diverticulitis coli (cDC), due to non-contained perforations.⁹ In cultures obtained from cDC patients anaerobic bacteria alone were present in 18%, aerobic bacteria alone in 5% and, more commonly, mixed aerobic and anaerobic flora in 77%. The predominant aerobic and facultative organisms

Address for Correspondence: Alaa El-Hussuna, MD,
Aalborg University Hospital, Department of Surgery, Aalborg, Denmark
E-mail: alaanewemail@gmail.com ORCID ID: orcid.org/0000-0002-0070-8362

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were *E. coli* and *Streptococcus* spp. Poly-microbial flora were recovered in 86% of patients.¹⁰ Therefore, broad-spectrum antibiotics are recommended. However, there is no consensus about antibiotic regimen in cDC.^{11,12} There is little evidence to suggest that oral antibiotics are as effective as intravenous antibiotics.¹³ The rate of relapse at 30 days following non-operative management of cDC was 18.9% and the rate of recurrence following non-operative management was 25.5% at a mean follow-up of 38 months.¹⁴

Few studies have compared the bacterial species identified in cultures from abscesses formed in patients with CD and cDC. The aim of this study was to investigate the microbiological profile in abscess fluids drained from patients with CD compared to intra-abdominal abscess fluid drained from patient with cDC.

Materials and Methods

This was a retrospective, cohort, pilot study. The cohort of patients had a diagnosis of CD or cDC and had undergone radiologically-guided, percutaneous drainage of intra-abdominal abscess in a single tertiary center (Aalborg University Hospital) in the period 2008-2019.

The primary objective was to investigate the microbiological profile of culture isolates obtained from intra-abdominal abscesses drained in patients with CD compared to those with cDC.

Patients

Adult patients who underwent radiologically-guided, percutaneous drainage, using either ultrasonography (US) or computed tomography (CT), as part of treatment were included. Aspiration of intra-abdominal abscesses was performed and samples from the drainage were cultured from patients in both the CD and cDC groups. Gram-staining was used to detect positive, negative and mixed species.

Data items included demographic data, pre-operative medications in the CD group, abscess size, antibiotic coverage after drainage, recurrence of abscess, surgical resection, type of resection and post-operative complications. Data items were collected and compared in the CD and cDC groups. Informed consent from individual patients was not deemed necessary because of the retrospective nature of the study. However, ethical approval to collect data was obtained from the Danish Agency (approval number: STPS 3-3013-3045/1).

Statistical Analysis

SPSS, version 27, was used for analysis of data (IBM Corp., Armonk, NY, USA). Continuous variables were reported using median and interquartile range (IQR). For univariate analysis, Pearson chi-square and Fisher's exact tests were

used for categorical variables and Mann-Whitney U test for continuous variables. A two-sided p-value less than 0.05 was considered statistically significant.

Due to the pilot nature of this study multivariate analysis was not done.

Results

A total of 44 patients with CD (n=18) and cDC (n=26) were investigated in this pilot study. Of 18 patients with CD, 10 (55.6%) were females and median IQR age at time of diagnosis was 32 (24.25-47.75) years. Similarly, among the 26 patients with cDC, 18 (69.2%) were females and median (IQR) age at diagnosis was 55.5 (39.5-62.25) years (Table 1). All patients underwent percutaneous, radiologically-guided drainage of an intra-abdominal abscess. The specimens were then cultured for determination of microbiological profile in both groups of patients.

There was a significant difference in median largest diameter of abscess between the two groups ($p=0.04$). Abscesses were larger in cDC with a median (IQR) largest diameter of 65 (42.5-78.75) mm compared to 40 (33.75-70) mm in patients with CD (Table 1).

There was no significant difference in antibiotic coverage in the two groups, in that all patients with CD and cDC received broad spectrum antibiotics prior to abscess drainage. However, there was a significant difference in other pre-operative medications, including steroids, immunosuppressive agents and biologics, with predominance of those medications in patients with CD ($p<0.001$) (Table 1).

Cultures after drainage were performed and results showed mostly mixed Gram-positive and Gram-negative bacteria in both groups, but in patients with cDC, there was a significantly higher proportion of cultures of Gram-negative bacteria only ($p=0.029$) (Figure 1, 2).

The most common bacterial spp. in cultures was *E. coli* in both groups of patients. Anaerobic bacteria were the second most common spp. in cDC, while *Streptococcus*, *Enterococcus*, extended spectrum beta lactamase (ESBL)-producing organisms, *Pseudomonas*, *Morganella* and *Proteus* were the second most common in patients with CD (Figure 1, 2). Recurrence of abscess was reported in 33.3% of patients with CD after radiologically guided percutaneous drainage compared to cDC patients who reported no abscess recurrence after drainage ($p=0.019$) (Table 2).

In patients with CD who underwent surgical resection, abscess was present at the time of surgery (50%), compared to 15.4% of cDC patients with abscess at time of surgery. Fistula was the most common post-operative complication

Table 1. Baseline demographic and medical characteristics of the patients in the Crohn's disease and diverticulitis coli groups prior to abscess drainage

	Crohn's disease, n=18/44 (40.9%)	Diverticulitis coli, n=26/44 (59.1%)	Univariate analysis, (p)
Demographics*			
Age, median (IQR), years	32 (24.25-47.75)	55.5 (39.5-62.25)	0.006
Gender (female)	10 (55.6%)	18 (69.2%)	ns
BMI, median (IQR), (kg/m ²)	21.95 (18.7-28.0)	26.2 (23.05-31.1)	0.02
DM, any type	1 (5.6)	2 (7.7)	ns
Insulin-dependent DM	0 (0)	1 (3.8)	ns
Non-insulin dependent DM	1 (5.6)	1 (3.8)	ns
Smoking, at any time	9 (50)	8 (30.8)	ns
Current smoker	8 (44.4)	5 (19.2)	ns
Ex-smoker	1 (5.6)	3 (11.5)	ns
Median (IQR) abscess size (mm)	40 (33.75-7)	65 (42.5-78.75)	0.046
Medical treatment before drainage			
Antibiotics	16 (88.9)	25 (96.2)	ns
Steroids	13 (72.2)	0 (0)	<0.001
Immunosuppressive therapy	9 (50)	0 (0)	<0.001
Biologics therapy	6 (33.3)	1 (3.8)	0.009

*All results are given as n (%) unless otherwise stated. IQR: Interquartile range, ns: Not significant, BMI: Body mass index, DM: Diabetes mellitus

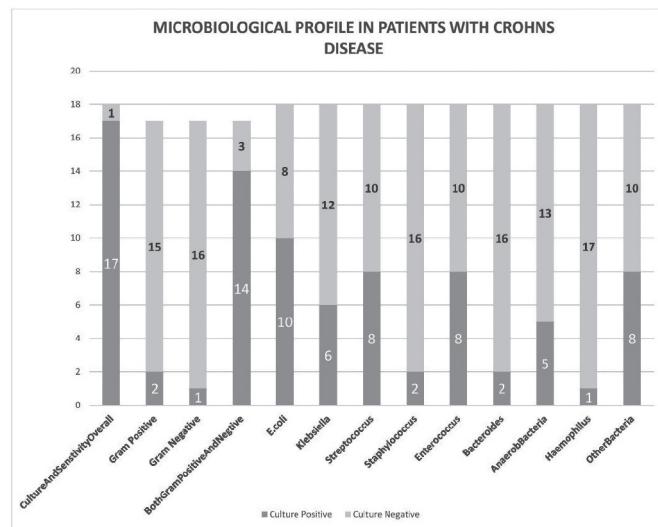


Figure 1. Microbiological profile in cohort of Crohn's patients who underwent radiologically guided percutaneous abscess drainage

reported for both groups. In the CD group, the second most common post-operative complication was ileus (commonly grade 2 ileus) and sepsis (commonly grade 2 sepsis) (21.4%). However, the second most common post-operative complications were superficial surgical site infection SSI (7.7%) in the cDC group (Table 3).

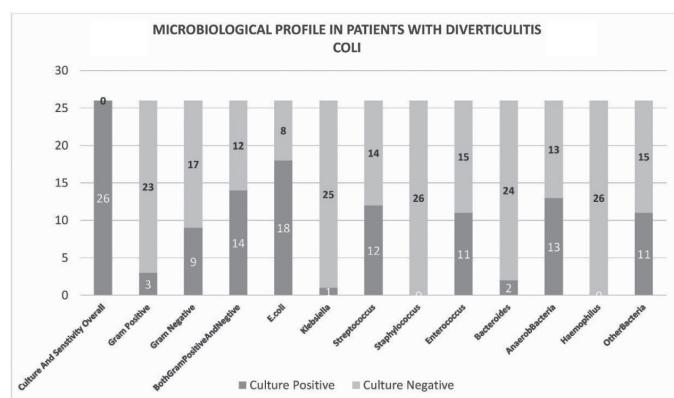


Figure 2. Microbiological profile in cohort of diverticulitis patients who underwent radiologically guided percutaneous abscess drainage

Discussion

This study demonstrated predominantly mixed Gram-positive and negative bacteria and *E. coli* in cultures recovered from abscesses in both CD and cDC patients. Both groups showed significant growth of *Enterococci*, *Streptococci* and anaerobic bacteria in culture from drained intra-abdominal abscesses.

These data confirm previous studies on types and species of bacteria in intra-abdominal abscesses in CD and cDC, in which *E. coli*, *Enterococci*, *Streptococci* and anaerobic

Table 2. Comparison of the Crohn's disease and diverticulitis coli groups after abscess drainage and microbiological profile of isolates following culture

	Crohn's disease, n=18/44 (40.9%)	Diverticulitis coli, n=26/44 (59.1%)	Univariate analysis, (p)
After drainage*			
Culture and sensitivity performed	17 (94.4)	26 (100)	ns
Gram-positive only	2/17 (11.8)	3 (11.5)	ns
Gram-negative only	1/17 (5.9)	9 (34.6)	0.029
Mixed Gram-positive and negative	14/17 (82.4)	14 (53.8)	ns
<i>E. coli</i>	10 (55.6)	18 (69.2)	ns
<i>Klebsiella pneumoniae</i>	6 (33.3)	1 (3.8)	0.009
<i>Streptococcus</i>	8 (44.4)	12 (46.2)	ns
<i>Staphylococcus</i>	2 (11.1)	0 (0)	ns
<i>Enterococcus</i>	8 (44.4)	11 (42.3)	ns
Bacteroides	2 (11.1)	2 (7.7)	ns
Anaerobic bacteria	5 (27.8)	13 (50)	ns
Haemophilus	1 (5.6)	0 (0)	ns
Other bacteria	8 (44.4)	11 (42.3)	ns
Hemoglobin level, median (IQR), (g/dL)	7.1 (6.4-8.5)	7.05 (6.275-7.65)	ns
Albumin level, median (IQR),	29 (27-37.5)	27 (23.5-30.5)	ns
Antibiotics coverage after drainage	17 (94.4)	26 (100)	ns
Recurrence of abscess	6 (33.3)	0 (0)	0.019

*All results are given as n (%) unless otherwise stated. IQR: Interquartile range, ns: Not significant

bacteria were reported to be the predominant pathogens.^{1,10} These findings were not surprising, as the origin of all these infections are the gastrointestinal flora. In addition, both groups of patients showed significant number of positive cultures for ESBL-producing organisms, probably due to bacterial resistance as a result of wide antibiotic coverage used in the treatment regimen for both conditions.¹⁵ However, patients with CD and using immunosuppressants were more likely to have an intra-abdominal infection caused by ESBL-producing bacteria.⁵ Immunosuppressive therapy was also associated with a markedly increased risk for development of intra-abdominal abscess in patients with CD.¹⁶

There was a significant difference in microbiological profile between the groups of patients in terms of *Klebsiella pneumoniae* culture, which was significantly more prevalent in the CD group. There is a general consensus that CD develops as the result of immune-mediated tissue damage triggered by infections with intestinal microbial agents. Based on the results of existing microbiological, molecular, and immunological studies, *Klebsiella pneumoniae* seems to have a key role in the initiation and perpetuation of the

pathological damage involving the gut and joint tissues in patients with CD.¹⁷ Abscess recurrence after drainage was also more commonly reported in CD, which again is expected due to the chronic inflammatory nature of CD in comparison to cDC.

Use of broad-spectrum antibiotics with coverage for Gram-positive, Gram-negative and anaerobic bacteria is mandatory for the treatment of cDC, that is diverticulitis with perforation and/or abscess. This type of antibiotherapy may be part of management in patients with CD, but our results suggest anti-*Klebsiella pneumoniae* antimicrobial agents, such as rifampicin, might be added to the treatment regimen.¹⁷

The primary limitation of this study was that it involved data from a single tertiary center, which may introduce referral bias and raises concerns of generalizability. Patients from referral centers often have more severe disease resulting in more frequent health care encounters, hospitalizations, surgeries, and use of immunosuppressive drugs and antibiotics, all factors which may affect the types of bacteria implicated in abscesses formed in these patients. Another important limitation was the small sample size and lack of

Table 3. Comparison of surgery and post-operative complications in the Crohn's disease and diverticulitis coli groups

	Crohn's disease n=18 (40.9)	Diverticulitis coli, n=26 (59.1)	Univariate analysis, (p)
After surgery			
Urgency (elective)	9/14 (64.3)	4/5 (80%)	ns
Resection	14/14 (100)	4 (15.4)	<0.001
Resection (small bowel)	1/14 (7.1)	0 (0)	ns
Resection (ileo-colic)	5/14 (35.7)	1 (3.8)	0.007
Resection (colectomy)	1/14 (7.1)	3 (11.5)	ns
Resection (sigmoid)	0/14 (0)	1 (3.8)	ns
Resection (combination)	7/14 (50)	0 (0)	ns
Abscess at time of surgery	7/14 (50)	4 (15.4)	0.019
Fistula	10/14 (71.4)	2 (7.7)	<0.001
Ileus, all	3/14 (21.4)	1 (3.8)	ns
Post-op ileus grade 1	1/14 (7.1)	1 (3.8)	ns
Post-op ileus grade 2	2/14 (14.3)	0 (0)	0.048
Post-op ileus grade 3b	0/14 (0)	1 (3.8)	ns
IASC, all	4/14 (28.6)	1 (3.8)	0.024
IASC grade 1	1/14 (7.1)	0 (0)	ns
IASC grade 2	1/14 (7.1)	0 (0)	ns
IASC grade 3a	1/14 (7.1)	0 (0)	ns
IASC grade 3b	1/14 (7.1)	1 (3.8)	ns
Deep SSI overall	0/14 (0)	1 (3.8)	ns
Deep SSI grade 3b	0/14 (0)	1 (3.8)	ns
SSI, all	0/14 (0)	2 (7.7)	ns
SSI grade 1	0/14 (0)	1 (3.8)	ns
SSI grade 3b	0/14 (0)	1 (3.8)	ns
Sepsis, all	3/14 (21.4)	1 (3.8)	ns
Sepsis grade 1	1/14 (7.1)	0 (0)	ns
Sepsis grade 2	2/14 (14.3)	0 (0)	0.048
Sepsis grade 3b	0/14 (0)	1 (3.8)	ns
Stoma, all	4/18 (22.2)	2 (7.7)	ns
End ileo-stomi	2/18 (11.1)	1 (3.8)	ns
End colostomi	2/18 (11.1)	1 (3.8)	ns
Complication rate	4/14 (28.6)	4 (15.4)	ns
LOS binary (<8 days)	11/18 (61.1)	25 (96.2)	0.003
Post-op re-admission	4/18 (22.2)	3 (11.5)	ns
Re-operation	4/18 (28.6)	2 (7.7)	ns

*All results are given as n (%). ns: Not significant, SSI: Surgical site infection

information regarding other types of bacteria, fungi and antibiotic sensitivity and resistance. Future large prospective studies are needed to explore the microbiological profile of abscess-dwelling organisms in CD and cDC patients.

Conclusion

Mixed Gram-positive and negative bacteria with *Escherichia coli* predominance were the most common bacteria culture in both groups. One notable finding was that *Klebsiella pneumoniae* was more commonly found in cultures from intra-abdominal abscesses drained from patients with CD compared to cultures of intra-abdominal abscess in patients with cDC. This suggests that a trial of adding a *Klebsiella*-specific antimicrobial agent to the antibiotic regimen used in these patients may be worthwhile.

Ethics

Ethics Committee Approval: However, ethical approval to collect data was obtained from the Danish Agency (approval number: STPS 3-3013-3045/1).

Informed Consent: Informed consent from individual patients was not deemed necessary because of the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.F.A.R., H.A., A.E.H., Concept: R.F.A.R., H.A., A.E.H., Design: R.F.A.R., H.A., A.E.H., Data Collection or Processing: R.F.A.R., H.A., A.E.H., Analysis or Interpretation: R.F.A.R., H.A., A.E.H., Literature Search: R.F.A.R., H.A., A.E.H., Writing: R.F.A.R., H.A., A.E.H., OpenSourceResearch is an international organization with a special focus on implementing information technologies and artificial intelligence in clinical research. The manuscript will be background material for other studies that the organization is planning to conduct, as shown on its website: <https://www.osrc.network>.

Conflict of Interest: No conflict of interest was declared by the authors.

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