

Microbiological Testing and Antibiotic Resistance in Patients Undergoing Drainage for Perianal Abscess: A Retrospective Observational Cohort Study

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IIIIIIII ABSTRACT |

Aim: Despite the widespread use of empiric antibiotics, the role of routine microbiological testing in patients with perianal abscesses to guide treatment remains uncertain. This study aimed to assess the rate of microbiological testing, the spectrum of pathogens identified, and their antibiotic resistance profiles in patients who underwent surgical drainage of perianal abscess.

Method: A single-center retrospective study was conducted on 141 adult patients who underwent incision and drainage for perianal abscesses between January 2017 and March 2024. The attending surgeon decided whether to obtain intraoperative bacteriological culture samples. Clinical characteristics, culture results, and antibiotic resistance profiles were analyzed.

Results: Microbiological testing was performed in 32.6% of patients. Bacterial isolates were detected in 63.0% of the tested patients, with *Escherichia coli* (*E. coli*)(52.2%) and *Klebsiella pneumoniae* (*K. pneumoniae*) (10.8%) being the most frequently isolated bacteria. Antibiotic resistance rates were high, particularly for *E. coli*, with resistance to ampicillin (81.4%) and cefazolin (75.0%) being the most common. No resistance was observed to amikacin, colistin, or carbapenems. At a median follow-up of 93 days, 68.8% of the patients reported no sequelae, whereas 19.9% required further surgical intervention for perianal fistula.

Conclusion: The results suggest that a considerable portion of perianal abscess cases harbor resistant pathogens, particularly *E. coli* and *K. pneumoniae*. Given the high rates of antibiotic resistance observed, routine microbiological testing may help guide targeted antibiotic therapy, especially in patients with complex or recurrent abscesses. Although microbiological testing revealed high resistance rates among common pathogens, the findings must be interpreted cautiously, given the retrospective design, limited use of microbiological testing, absence of anaerobic cultures, and delayed result availability.

Keywords: Perianal glands, abscess, aerobic bacteria, Escherichia coli, Klebsiella pneumoniae, antibacterial drug resistance

Introduction

A perianal abscess is an acute suppurative infection of the soft tissue surrounding the rectum and anus. ¹ It is a common condition encountered in emergency general surgery. ² The primary underlying cause is the inflammation of the anal glands at the base of the anal crypts, a condition known as

cryptoglandular origin.^{3,4} Systemic infection or life-threatening sepsis may occur, notably in elderly patients or those with compromised immune systems.¹ Although timely drainage of the abscess is the most effective treatment modality, empiric antibiotic treatment, regardless of culture results, is usually recommended to control cellulitis, systemic illness, or underlying immunosuppression. Depending on the



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Received: 22.04.2025 Accepted: 10.08.2025 Epub: 19.11.2025

Cite this article as: Bölük SE, Bölük S, Karatepe YK, Şenol Z. Microbiological testing and antibiotic resistance in patients undergoing drainage for perianal abscess: a retrospective observational cohort study. Turk J Colorectal Dis.



localization, a perianal fistula is the major complication of a perianal abscess.^{1,2}

The most common pathogens detected in patients with perianal abscesses include a mix of aerobic and anaerobic gut microbiota, such as Escherichia coli (E. coli), Proteus vulgaris, and Staphylococcus aureus, as well as Streptococcus, Bacteroides, and Peptostreptococcus species. 1,3,5 However, conventional culturebased diagnostic techniques may be limited in covering the full microbial spectrum in such infections.1 Additionally, antimicrobial drug resistance has been increasingly reported. 6,7 Despite these concerns, there is ongoing debate regarding the utility of routine microbiological testing, particularly in uncomplicated abscesses, where empirical management is often sufficient, outcomes are generally favorable, and culture data rarely alter immediate management in straightforward cases. Given these limitations, several authors have questioned the need for routine microbiological examination of pus swabs from uncomplicated perianal abscesses.7-9 Although some earlier studies suggested a link between gut microbiota in perianal abscess cavities and subsequent fistula development, more recent evidence does not consistently support this association.^{9,10} Consequently, according to the drainage culture test results, the optimum antibiotic regimens remain speculative.7,9,11

This study primarily aimed to determine the rate of microbiological testing, describe the microbiological and resistance profile of perianal abscesses in a surgical cohort, and assess potential implications for empirical antibiotic choice.

Materials and Methods

Study

A single-center retrospective, observational cohort study was conducted on patients who underwent surgical treatment with incision and drainage for perianal abscesses in the general surgery clinics of a tertiary referral center in İstanbul, Türkiye, between January 2017 and March 2024. The local ethics committee of University of Health Sciences Hamidiye Scientific Research Ethics Committee approved the study (approval number: 2/26, dated: 16.02.2024) which adhered to the principles outlined in the Declaration of Helsinki. Written informed consent was waived due to the study's retrospective design and the anonymity of the data.

Patients

All consecutive hospitalized adult patients aged 18 years or older who underwent an incision and drainage procedure for a perianal abscess were retrospectively identified through the hospital's medical records system. Patients treated conservatively and those with incomplete clinical and follow-up data were excluded from the study. Further exclusion criteria included patients with inflammatory bowel disease

(n=2), perianal abscesses associated with tumoral lesions (n=1), and Fournier's gangrene (n=10). Patients with recurrent perianal abscesses were included in the study. In total, 141 patients were included in the study (Figure 1).

Treatment and Procedure

The attending surgeon initiated perioperative empirical antibiotic treatment for all patients with β-lactam/βlactamase inhibitors or fluoroquinolones, supplemented with metronidazole. Intraoperatively, bacteriological culture samples were obtained using either a swab stick or by aspirating pus from the abscess after incision at the area of most fluctuation.9 The decision to perform microbiological testing was at the discretion of the attending surgeon. At our institution, there was no standardized protocol guiding the decision to obtain culture samples; this decision was based solely on the surgeon's clinical judgment. Bacterial cultures obtained from the perianal abscess cavity were cultured under aerobic conditions in the hospital's microbiology laboratory. All patients were discharged 24-48 hours after the procedure, receiving oral antibiotics similar to those administered perioperatively. Antibiotic regimens could not be adjusted based on antibiogram results, as microbiology findings typically became available within 48-72 hours, after the patients who underwent microbiological testing had already been discharged from the hospital.8

Variables and Data Collection

Patient demographics, including age, sex, weight, height, comorbidities, history of perianal surgical interventions, and microbiological test results with antibiograms (if performed), were retrospectively collected from medical records. The body mass index was calculated by dividing the weight by the height squared (kg/m²). The results of the microbiological testing were categorized as negative, contamination, or positive.

Follow-Up

Follow-up data were collected using the patient's medical records or via a telephone call performed in July 2024. All patients were requested to attend regular monthly visits at the outpatient general surgery clinics for the first 6 months following surgery. The perianal abscess and/or perianal fistula outcomes were noted as cure, perianal drainage from the fistulous tracts without intervention, or surgical treatment of perianal fistula.

Statistical Analysis

The primary outcome of the study was the rate of microbiological testing, the main exposure of interest. The grouping was based on the presence of microbiological testing. The microbiological and antibiotic resistance profiles of perianal abscesses among patients with microbiological testing were the secondary outcomes.

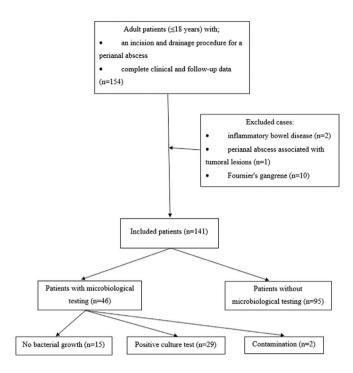


Figure 1. Flowchart of the study

For descriptive statistics, the mean ± standard deviation was used to present continuous data with a normal distribution. The median with minimum and maximum values was applied for continuous variables without a normal distribution. Numbers and percentages were used for categorical variables. The Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests were used to analyze the normal distribution of the numerical variables.

To compare the differences in numerical variables between the two independent groups, the independent samples t-test was used for numerical variables that were determined to conform to the normal distribution. The Mann-Whitney U test was used for numerical variables determined not to conform to the normal distribution. The categorical variables were compared using Pearson's chi-square test or Fisher's exact test as appropriate.

Data were analyzed using SPSS Statistics for Windows (IBM Corp., IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA). The significance level (p-value) was determined at 0.05 in all statistical analyses.

Results

There were 141 patients, with a mean age of 40.8±13.0 years. Most patients were men (78.7%). Thirty-five patients (24.8%) had a history of perianal abscess and/or fistula, with 82.9% of these cases involving a prior perianal abscess. Additional clinical characteristics are summarized in Table 1.

Microbiological testing was performed on 46 patients (32.6%). Of these, 15 patients (32.6%) had no bacterial growth, whereas 29 patients (63.0%) had positive culture results. Polymicrobial infections were identified in three patients (6.5%). The most frequently detected bacterium was *E. coli*, found in 24 patients (52.2%), followed by *Klebsiella pneumoniae* (*K. pneumoniae*) in five patients (10.8%). The rates of the other bacteria are given in Table 2.

The comparison of patients with and without microbiological testing revealed no significant differences in demographic and clinical characteristics (p>0.05) (Table 3).

At a median follow-up of 93 days after discharge, 97 patients (68.8%) reported no complications or recurrence (Table 4). However, 15 patients (10.6%) experienced perianal drainage with varying intensity and frequency. Additionally, 29 patients (20.6%) required surgical intervention for a diagnosed perianal fistula.

The antibiotic resistance rates of *E. coli* and *K. pneumoniae* to standard antibiotics are shown in Table 5. The highest drug resistance for *E. coli* was detected with ampicillin (81.4%) and cefazolin (75.0%). Antibiotic resistance to *E. coli* was also observed with cefuroxime (61.1%), levofloxacin (60.0%), ceftazidime (59.1%), amoxicillin/clavulanate (55.6%), and ceftriaxone (55.6%). No drug resistance was observed with amikacin, colistin, meropenem, imipenem, or tigecycline for *E. coli*. The antibiotic susceptibility and resistance rates of *K. pneumoniae* are summarized in Table 5.

Table 1. Demographic and clinical characteristics of the patients (n=141)

(11=171)		
Variable		Value
Age (years) [†]		40.8±13.0
Sex [‡]	Male	111 (78.7)
	Female	30 (21.3)
Body mass index (kg/m²)†		28.0±4.7
Comorbidities [‡]		54 (38.3)
Type of comorbidity [‡]		
	Hypertension	21 (14.9)
	Diabetes mellitus	22 (15.6)
	Coronary artery disease	6 (4.3)
	COPD	6 (4.3)
History of perianal abscess/fistula [‡]		35 (24.8)
	Perianal abscess	29 (82.9)
	Perianal fistula	7 (17.1)
Previous perianal other surgeries [‡]		10 (7.1)

†: mean ± standard deviation, ‡: n (%)

COPD: Chronic obstructive pulmonary disease

Table 2. Details of the patients with microbiological analysis (n=46)

Variable		Value
Test results [‡]	No growth	15 (32.6)
	Contamination	2 (4.3)
	Positive	29 (63.0)
Polymicrobial abscess [†]		3 (6.5)
Pathogenic bacteria ^{‡, ζ}	E. coli	24 (52.2)
	K. pneumoniae	5 (10.8)
	E. fecalis	1 (2.2)
	S. aureus	1 (2.2)
	N. gonorrhea	1 (2.2)

‡: n (%)

^ζ: 32 isolated bacteria in 29 patients with positive test results

E. coli: Escherichia coli, K. pneumoniae: Klebsiella pneumoniae, E. fecalis: Enterococcus faecalis, S. aureus: Staphylococcus aureus, N. gonorrhea: Neisseria gonorrhoeae

Discussion

This retrospective study's findings revealed that microbiological testing was performed in nearly one-third of the patients undergoing surgical drainage for perianal abscesses. Positive cultures were obtained in 63% of the tested individuals, with E. coli and K. pneumoniae being the most frequently cultured bacteria. However, the high rates of antibiotic resistance observed in these organisms highlight the need for careful consideration when selecting appropriate antibiotic therapy. The routine use of swab cultures in the management of perianal abscesses has been debated in previous studies, with sampling rates ranging from 41.8% to 78%.^{2,6,8,9,11} Seow-En I and Ngu J. 11 suggested that such procedures may be unnecessary due to their minimal impact on patient management and outcomes. In their study, 78% of patients underwent microbiological testing, yet physicians did not review 96.5% of these results. Similarly, in a study involving 24 patients with perianal abscesses, only one-third of microbiological test results were reviewed by attending physicians.8 Another study, including pediatric cases with pilonidal, gluteal, and perianal abscesses, reported that routine culture did not appear to alter treatment.⁷ Additionally, several authors have reported no significant association between the presence of gut organisms and the development of fistulas or the recurrence of abscesses.^{8,9} In line with these findings, the relatively low microbiological testing rate (32.6%) in our study likely reflects individual physician discretion rather than adherence to a standardized protocol or institutional guidelines. Swab cultures were not routinely recommended as part of clinical practice during the study period. Many clinicians may have chosen not to obtain cultures in the absence of systemic signs of infection or recurrent disease. Resource considerations may also have contributed, particularly when microbiological results were unlikely to impact clinical decision-making. Although we did not analyze the rate of review or subsequent treatment modifications based on test results, prospective studies could better elucidate the potential benefits of microbiological sampling in these patients.

Earlier research has demonstrated that *E. coli* is the predominant pathogen in perianal abscesses across various age groups and diagnostic techniques. ^{1-3,12,13} Zhu and Xu¹⁴ found that *K. pneumoniae* was the predominant pathogen in infants under 3 months of age with perianal abscesses. Nevertheless, Liu et al. ⁵ found that *E. coli* was detected in 65% of 183 patients with perianal abscesses. They also categorized the study group based on the presence of diabetes mellitus. *Klebsiella pneumoniae* was more frequent than *E. coli* among people

Table 3. Demographic and clinical characteristics of the patients with and without microbiological testing

	Patients		
	With microbiological testing (n=46)	Without microbiological testing (n=95)	p
	39.3±10.3	41.5±14.2	0.294
ale	38 (82.6)	73 (76.8)	0.514
male	8 (17.7)	22 (23.2)	
	27.4±5.3	27.1±4.4	0.689
	15 (32.6)	39 (41.1)	0.361
ypertension	4 (8.7)	17 (17.9)	0.208
abetes mellitus	6 (13.0)	16 (16.8)	0.629
oronary artery disease	2 (4.3)	4 (4.2)	1.0
OPD	1 (2.2)	5 (5.3)	0.664
	14 (30.4)	21 (22.1)	0.304
rianal abscess	13 (92.9)	16 (76.2)	0.125
rianal fistula	1 (2.2)	5 (23.8)	0.427
	1 (2.2)	9 (9.5)	0.166
	13 (28.3)	14 (14.7)	0.069
y	rpertension abetes mellitus bronary artery disease DPD	With microbiological testing (n=46) 39.3±10.3 38 (82.6) male 8 (17.7) 27.4±5.3 15 (32.6) Pertension 4 (8.7) abetes mellitus 6 (13.0) ronary artery disease 2 (4.3) PPD 1 (2.2) 14 (30.4) rianal abscess 13 (92.9) rianal fistula 1 (2.2) 1 (2.2)	With microbiological testing (n=46) Without microbiological testing (n=95) 39.3±10.3 41.5±14.2 38 (82.6) 73 (76.8) male 8 (17.7) 22 (23.2) 27.4±5.3 27.1±4.4 15 (32.6) 39 (41.1) abetes mellitus 6 (13.0) 16 (16.8) aronary artery disease 2 (4.3) 4 (4.2) DPD 1 (2.2) 5 (5.3) 14 (30.4) 21 (22.1) rianal abscess 13 (92.9) 16 (76.2) rianal fistula 1 (2.2) 5 (23.8) 1 (2.2) 9 (9.5)

^{†:} mean ± standard deviation, †: n (%)

COPD: Chronic obstructive pulmonary disease

Table 4. Outcome of the patients in the study group (n=141)

Variable		Value	
Follow-up (days)§		93 (3-2347)	
Outcome [‡]	No sequelae	97 (68.8)	
	Recurrences	44 (31.2)	
	Symptoms for perianal fistula		15 (34.1)
	Surgery for perianal fistula		29 (65.9)

^{§:} median (min-max), †: n (%)

with diabetes, contrary to the findings obtained by Alabbad⁶, in which *E. coli* was the most common pathogen in patients with and without diabetes mellitus. Others used the term "gut organisms" without reporting the names or incidences of the specific pathogens.⁹ In line with previous findings, *E. coli* was the most frequently isolated pathogen in our study, followed by *K. pneumoniae*. Nevertheless, the relatively small number of cultured pathogens may limit the comprehensiveness of our bacteriological findings.

Antibiotic sensitivity results for bacteria isolated from perianal abscesses have varied across studies. In the study by Liu et al.⁵, *E. coli* isolates were susceptible to first-generation cephalosporins, with rates of 84.6% in patients with diabetes and 65.1% in

patients without diabetes. Similar findings have been reported by Seow-En and Ngu¹¹, who found that 98% of isolated organisms were sensitive to routine empirical antibiotics, such as amoxicillin/clavulanic acid and metronidazole. Contrary to these findings, Bender et al.² reported that acquired drug resistance to common antibiotics for *E. coli*, *S. aureus*, and *Bacteroides* and *Streptococcus* species was frequently seen in patients with perianal abscesses. Due to the varying drug resistance rates in children with perianal abscesses, Guner Ozenen et al.³ found the highest antimicrobial coverage rate with ertapenem plus a glycopeptide, followed by ertapenem plus clindamycin. In the current study, we observed conflicting findings: *E. coli* and *K. pneumoniae* were more likely

Table 5. Antibiotic resistance rates of E. coli and K. pneumoniae in the bacterial culture of perianal abscess

Antibiotic	E. coli*	K. pneumoniae*
Amikacin	20/0 (0)	3/0 (0)
Amoxicillin/clavulanic acid	18/10 (55.6)	2/1 (50)
Ampicillin	17/14 (82.4)	2/2 (100)
Ertapenem	16/1 (6.3)	3/0 (0)
Gentamycin	19/3 (15.8)	1/0 (0)
Colistine	13/0 (0)	3/0 (0)
Meropenem	12/0 (0)	4/0 (0)
Imipenem	9/0 (0)	
Piperacillin/tazobactam	21/1 (4.8)	5/2 (40.0)
Cefazolin	12/9 (75.0)	1/1 (100)
Cefoxitin	17/4 (25.5)	3/0 (0)
Cefuroxime	18/11 (61.1)	3/1 (33.3)
Ceftazidime	22/13 (59.1)	4/1 (25.0)
Ceftriaxone	18/10 (55.6)	3/1 (33.3)
Cefepim	19/9 (47.4)	4/1 (25.0)
Ciprofloxacin	22/8 (36.4)	3/1 (33.3)
Levofloxacin	5/3 (60.0)	
Tigecycline	20/0 (0)	3/0 (0)
Trimethoprim/sulfamethoxazole	22/7 (31.8)	4/0 (0)
Aztreonam	7/2 (28.6)	2/0 (0)

^{*:} Number of isolates tested/number of resistant isolates (%), E. coli: Escherichia coli, K. pneumoniae: Klebsiella pneumoniae

to be resistant to cephalosporins and amoxicillin/clavulanic acid. These findings suggest that standard empiric antibiotics may be insufficient for treating perianal abscesses, given the relatively high resistance rates observed among the isolated pathogens. Although routine post-drainage antibiotic use has been debated in various studies^{10,15,16}, we, along with others, advocate for routine microbiological testing and treatment adjustments based on culture results, especially in cases with complex or severe local disease.²

The high antibiotic resistance rates observed in our study, particularly the 81.4% resistance to ampicillin and 75.0% resistance to cefazolin among *E. coli* isolates, raise important questions about current empiric therapy protocols. Traditional first-line empiric regimens, consisting of β -lactam/ β -lactamase inhibitors or fluoroquinolones with metronidazole, may be inadequate in settings with high resistance rates, as reported in other studies.² Our findings revealed high resistance rates

of *E. coli* and *K. pneumoniae* to commonly used empiric antibiotics such as ampicillin, amoxicillin/clavulanate, and several cephalosporins. These resistance patterns suggest that such antibiotics may not be appropriate for empirical use in patients with perianal abscesses in our setting. In contrast, carbapenems, tigecycline, amikacin, and colistin showed excellent in vitro activity against the isolated strains, though their use should be reserved for selected cases due to concerns about broad-spectrum overuse.

Although our data are limited to aerobic cultures from a single center and do not constitute a formal institutional antibiogram, they may still serve as a valuable reference for empirical antibiotic selection in similar clinical contexts. These findings support the integration of local microbiological surveillance into antibiotic stewardship initiatives to guide empiric therapy and reduce inappropriate use of broad-spectrum agents. Accordingly, institutions should consider revising their

empiric antibiotic protocols based on local resistance patterns and established antimicrobial stewardship principles.

Given the observed resistance patterns, several therapeutic strategies warrant consideration in high-resistance settings. First, empiric therapy could be escalated to include broader-spectrum agents such as piperacillin/tazobactam, which demonstrated only 4.8% resistance among *E. coli* isolates in our study. Second, the universal sensitivity to carbapenems, amikacin, and colistin suggests these agents could be reserved for severe cases or those with known risk factors for multidrug-resistant organisms. However, the routine use of such broadspectrum antibiotics must be balanced against the risk of further promoting antimicrobial resistance and increased healthcare costs.

This study has several limitations. Although the cohort represented a convenience sample of all eligible patients over 7 years, and no power calculation was performed as the study was exploratory and descriptive in nature, our findings may not be fully generalizable due to the single-center retrospective design and the limited number of patients undergoing microbiological testing. The retrospective design also limited our ability to gather reliable data on preoperative and postoperative antibiotic use, patient compliance, adverse effects, and longterm outcomes. The absence of a standardized protocol for culture sampling introduces selection bias, as the decision was based on individual surgeon preference rather than objective criteria. Furthermore, our microbiological testing was limited to aerobic culture conditions, which may have resulted in an underrepresentation of anaerobic pathogens commonly associated with perianal abscesses. Additionally, the delayed availability of culture results in routine clinical settings may have further limited their utility in guiding immediate treatment decisions. Importantly, there was no predefined protocol to modify or tailor antibiotic therapy based on culture findings, which restricted the potential clinical impact of microbiological testing. This methodological limitation is consistent with routine clinical practices in many institutions but should be addressed in future studies using more comprehensive culture techniques or molecular diagnostics. Moreover, although we observed significant resistance patterns in some isolated pathogens, our study design does not allow us to establish a causal relationship between specific microbiological findings and clinical outcomes, such as treatment failure or fistula formation. The inability to evaluate the relationship between antibiotic resistance and clinical outcomes, such as recurrence or fistula formation, represents another limitation of this study. This was primarily due to the heterogeneity of bacterial isolates and the lack of standardized microbiological testing throughout the 7-year study period. Additionally, the follow-up period in our study was limited to a median of 93 days, which may not be sufficient to evaluate

longer-term outcomes, such as delayed fistula recurrence, chronic symptoms, or antibiotic-related complications. Future studies should incorporate standardized long-term follow-up to assess these outcomes more accurately.

Future prospective multicenter studies using anaerobic or metagenomic approaches are needed to better evaluate the role of microbiological testing and the impact of tailored antibiotic therapy on clinical outcomes in patients with perianal abscesses. These studies should also consider the cost-effectiveness and potential benefits of culture-guided therapy, especially in patients at a higher risk of complications.

The generalizability of our findings may be limited due to the single-center, retrospective nature of the study and the specific patient population treated at our institution. Our cohort primarily consisted of adult patients managed at a tertiary care hospital, which may not fully represent patients treated in community settings or other healthcare systems with different empirical antibiotic protocols. Additionally, microbiological testing was not performed systematically, and anaerobic cultures were not included, potentially leading to an incomplete representation of the microbial spectrum encountered in perianal abscesses. Regional differences in antibiotic resistance patterns may also limit the external applicability of our results, as resistance profiles are known to vary substantially between geographic areas and healthcare institutions. Therefore, although our findings provide valuable insight into local resistance trends and the utility of microbiological testing, they should be interpreted with caution when applied to other settings, and multicenter studies are warranted to validate these observations.

In conclusion, *E. coli* and *K. pneumoniae* were the most frequently identified pathogens in patients undergoing surgical drainage for perianal abscesses. Although microbiological testing was performed in nearly one-third of the patients, significant antibiotic resistance rates were observed in these bacteria, particularly to commonly used empiric antibiotics such as cephalosporins and amoxicillin/clavulanic acid. These findings highlight the presence of antibiotic-resistant organisms in perianal abscesses. However, given that microbiological results did not routinely inform treatment decisions in our study, the potential clinical benefit of culture-guided therapy remains uncertain. Future research is needed to determine whether tailoring antibiotics based on culture results improves outcomes in high-risk patient groups.

Ethics

Ethics Committee Approval: The local Ethics Committee of University of Health Sciences Hamidiye Scientific Research Ethics Committee approved the study (approval number: 2/26, dated: 16.02.2024) which adhered to the principles outlined in the Declaration of Helsinki.

Informed Consent: Written informed consent was waived due to the study's retrospective design and the anonymity of the data.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.E.B., Y.K.K., Z.Ş., Concept: S.B., Z.Ş., Design: S.E.B., Data Collection or Processing: S.E.B., Y.K.K., Analysis or Interpretation: A.H., Literature Search: S.B., Y.K.K., Z.Ş., Writing: S.E.B.

Conflict of Interest: There is no conflict of interest.

Financial Disclosure: There is no funding declaration for this manuscript.

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