

Original Article



Scalp Bacterial Profile and Antibiotics Susceptibility Pattern in Patients With Primary Cicatricial Alopecia

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ABSTRACT

Background: Primary cicatricial alopecia (PCA) is a group of disorders causing irreversible hair loss because of hair follicle destruction. Although bacterial colonization is suspected to contribute to PCA pathogenesis, its role remains unclear.

Objective: To investigate bacterial colonization patterns and antibiotic susceptibility profiles in patients with PCA compared to those with non-inflammatory scalp conditions.

Methods: This retrospective study analyzed bacterial cultures from scalp swabs of 161 subjects (68 patients with PCA and 93 controls) at a tertiary hospital between June 2011 and December 2023. Bacterial species and antibiotic resistance rates were evaluated using subgroup analyses of neutrophilic PCA (NCA).

Results: PCA cultures showed a higher prevalence of *Staphylococcus aureus* (24.3%) and *S. lugdunensis* (8.1%) than controls, where *S. capitis* (54.5%) was predominant. Gram-negative bacteria were more frequent in the PCA group (13.5%) than in the control group (9.9%), with *Klebsiella* spp. (10.9%) being the most prevalent. Resistance rates were significantly higher in PCA for benzylpenicillin, fusidic acid, erythromycin, clindamycin, oxacillin, and telithromycin ($p < 0.05$). Methicillin-resistant *S. aureus* was identified in 15% of *S. aureus* isolates from NCA cases. Gram-negative bacteria in PCA also exhibited increased resistance to ampicillin and ampicillin/sulbactam.

Conclusion: PCA exhibits distinct bacterial colonization and elevated antibiotic resistance, particularly in the neutrophilic subtypes. Bacterial culture and susceptibility testing are essential for targeted therapies in clinical practice. Further multicenter microbiome analyses with mechanistic studies are needed to elucidate bacterial contributions to PCA pathogenesis.

Keywords: Alopecia; Antibiotic resistance; Bacterial infections; Folliculitis; *Klebsiella*; Scalp dermatoses; *Staphylococcus aureus*

INTRODUCTION

Cicatricial (scarring) alopecia encompasses a group of disorders characterized by the irreversible destruction of hair follicles, resulting in permanent hair loss. Primary cicatricial alopecia (PCA), a subset of these conditions, occurs without secondary triggers such as burns, infections, or radiation. PCA is clinically characterized by the loss of hair follicle openings with accompanying

inflammatory signs such as erythema, pustules, and exudates, depending on the degree of inflammation^{1,2}. Based on the predominant inflammatory cell type, PCA is primarily classified into lymphocytic, neutrophilic, or mixed types³. The lymphocytic type includes lupus erythematosus and lichen planus, whereas the neutrophilic type includes folliculitis decalvans (FD) and dissecting cellulitis (DC)^{4,5}. FD typically involves painful purulent follicular exudation and tufting of hair, whereas DC is characterized by firm

or fluctuant nodules.

Despite extensive research, PCA pathogenesis remains poorly understood, posing a significant challenge for effective management^{1,2,4}. Current evidence suggests a multifactorial etiology, including the loss of follicular stem cells, genetic predispositions, and lipid metabolism dysregulation. Bacterial colonization and superinfection, particularly by *Staphylococcus aureus*, are increasingly implicated as contributors to disease progression, potentially through mechanisms such as superantigen-mediated hypersensitivity, particularly in the neutrophilic type^{2,6}. Treatments for PCA often include anti-inflammatory agents and antibiotics, such as tetracycline and clindamycin. However, the role of bacteria in PCA pathogenesis has not been adequately characterized.

Although prior studies have explored bacterial colonization in PCA, they largely focused on *S. aureus* and lacked a comprehensive analysis of bacterial diversity or antibiotic resistance patterns. Our study addresses these gaps by investigating bacterial colonization profiles and antibiotic susceptibility in PCA compared to non-inflammatory healthy scalp conditions.

MATERIALS AND METHODS

Patient characteristics

This study was conducted at Jeonbuk National University Hospital (JNUH) from June 12, 2011 to December 12, 2023. This study was approved by the Institutional Review Board (IRB) of JNUH (IRB

No. JNUH-2023-03-035) and adhered to the principles outlined in the Declaration of Helsinki.

The study included patients with hair loss and healthy volunteers (HV) who underwent bacterial scalp swab culture at a dermatology outpatient clinic. Diagnoses were confirmed through clinical evaluations, dermoscopic findings, and histopathological examinations in all patients with PCA and those with uncertain diagnosis. Based on these assessments, the participants were classified into 2 groups: PCA (patients with active, inflammatory PCA) and non-inflammatory healthy scalp controls. The control group included HV and patients with telogen effluvium (TE), androgenetic alopecia (AGA), or alopecia areata (AA). PCA samples were obtained from the affected areas across various scalp sites, whereas control samples were obtained from the unaffected occipital scalp. To minimize the influence of subclinical scalp inflammation on bacterial colonization, control participants were screened for erythema, scaling, or follicular inflammation; only those without clinical signs of active inflammation were included. Exclusion criteria included other inflammatory scalp conditions caused by infections, scalp dermatoses, drugs, or systemic diseases (Fig. 1).

Demographic and clinical data, including age, sex, duration of symptoms, alopecia subtype, primary clinical findings at sampling sites, prior treatment history, antibiotic use within the previous 3 months, and relevant comorbidities, were collected. The clinical morphology of the scalp including erythema, scaling, pustules, crusts, and tufted hair was recorded.

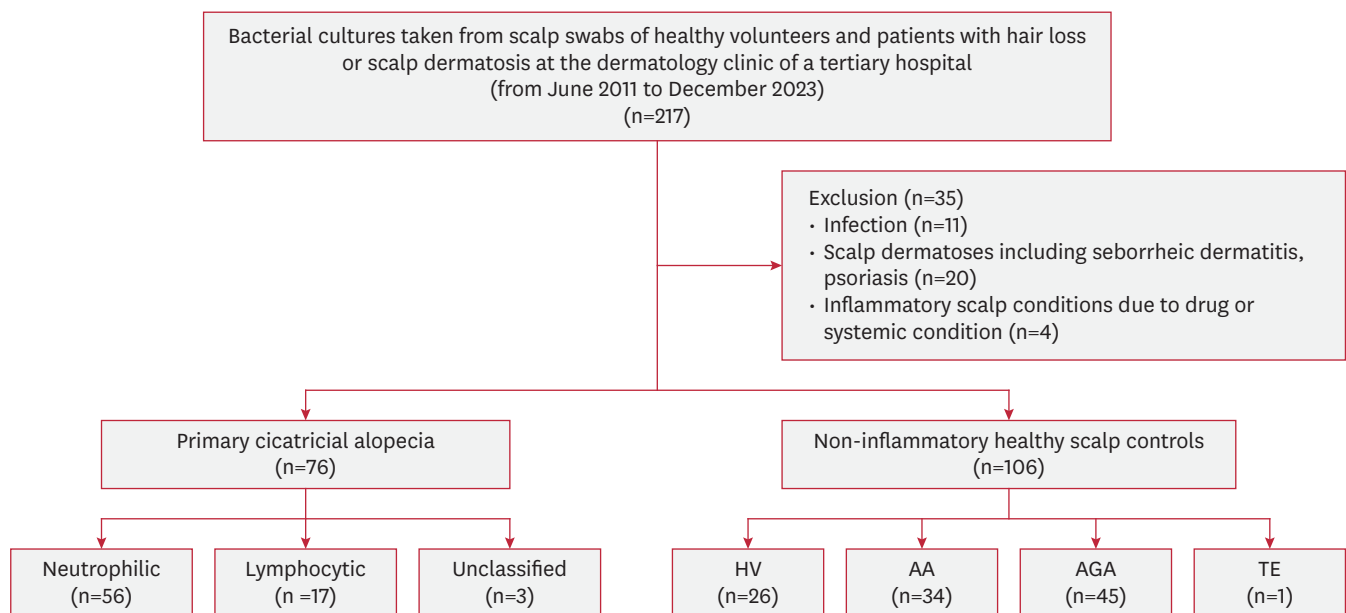


Fig. 1. Flow chart of this study.

HV: healthy volunteers, AA: alopecia areata, AGA: androgenetic alopecia, TE: telogen effluvium.

Scalp bacterial culture and antimicrobial susceptibility testing

Swab samples were collected from the scalps of the participants using sterile stick swabs with transport medium (Transport Media [1S]; Asanpharm, Seoul, Korea). Bacterial identification was conducted using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (VITEK-MS; BioMérieux, Marcy-l'Étoile, France) following the manufacturer's protocol. The results were interpreted using breakpoints established by the Clinical and Laboratory Standards Institute (CLSI).

The predominant cultured bacterial strain was analyzed for each patient. In cases in which 2 predominant strains were identified ($n=20$), both were included in the analysis. To ensure data accuracy, follow-up culture results from the same patients were excluded, thereby limiting the dataset to one result per patient. The bacterial culture findings were classified into gram-positive or gram-negative strains. Comparisons were made between the PCA and control groups, and separate subgroup analyses were conducted for neutrophilic PCA (NCA). Additionally, bacterial colonization was compared within control groups, between AGA, AA, TE, and HV.

Antimicrobial susceptibility testing was performed using the disc diffusion method according to the CLSI guidelines. The antibiotic resistance profiles of gram-positive and gram-negative bacteria were analyzed separately. Susceptibility was categorized as sensitive, intermediate, or resistant. Resistance rates were calculated as follows: Resistance Rate (%) = Number of Resistant Strains/Total Number of strains $\times 100$.

Statistical analysis

Statistical analyses were performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA). Categorical variables such as the proportion of cultured bacterial species between the PCA and control groups and within the control groups were analyzed using the χ^2 test. Demographic and clinical variables between the 2 groups were also compared using the 2-tailed Student's t -test and χ^2 test.

To minimize confounding bias, adjustments were made to key variables (e.g., prior antibiotic use). To ensure data integrity, patients with incomplete demographic or culture data were excluded. A p -value of <0.05 was considered statistically significant. To control the false discovery rate (FDR) and minimize false positives, the Benjamini-Hochberg method was applied where appropriate.

RESULTS

Demographics of the participants

The mean age of participants was 30.9 ± 14.1 years (PCA group: 31.9 ± 16.1 years; controls: 30.2 ± 12.4 years). Of the 161 participants, 101 (62.7%) were male, and 60 (37.3%) were female. In the PCA group, there were 47 male (69.1%) and 21 female participants (30.9%) compared with 54 male (58.1%) and 39 female participants (41.9%) in the control group. The comorbidities in patients with PCA included hypertension (7.4%), diabetes mellitus (4.4%), and hyperlipidemia (2.9%), with no significant differences in comorbidities, age, or sex between the PCA and control groups ($p > 0.05$) (Table 1).

Clinical characteristics of patients with PCA

Of the 68 patients with PCA, 26.5% (18/68) had lymphocytic PCA, including lichen planopilaris/frontal fibrosing alopecia (10.3%), central centrifugal cicatricial alopecia (7.4%), and lupus erythematosus (4.4%). The remaining 73.5% (50/68) of the patients had NCA, comprising FD (39.7%) and DC (33.8%). Twenty-six patients with PCA (38.2%) reported antibiotic use in the previous 3 months. The clinical features included erythematous macules/patches (98.5%), scales or dandruff (55.9%), pustules/abscesses (45.6%), and oozing or crusting (38.2%). Notably, 23 patients (33.8%) exhibited hair tufting. The duration of the disease varied, with 7.4% of the patients experiencing symptoms for <3 months, 11.8% for 3 months to 1 year, 27.9% for 1 to 3 years, and 52.9% for >3 years (Table 2).

Table 1. Demographics of the study participants

Demographic feature	Total (n=161)	Primary cicatricial alopecia (n=68)	Healthy scalp controls (n=93)	p-value
Age (yr)				0.453
Mean $\pm$ SD	5–75 (30.9 $\pm$ 14.1)	5–62 (31.9 $\pm$ 16.1)	7–75 (30.2 $\pm$ 12.4)	
Sex				0.205
Male	101 (62.7)	47 (69.1)	54 (58.1)	
Female	60 (37.3)	21 (30.9)	39 (41.9)	
Comorbidities				0.742
Hypertension	12 (7.5)	5 (7.4)	7 (7.5)	
Diabetes mellitus	8 (5.0)	3 (4.4)	5 (5.4)	
Hyperlipidemia	8 (5.0)	2 (3.0)	6 (6.5)	

Values are presented as number (%).
SD: standard deviation.

Bacterial Culture in Primary Cicatricial Alopecia

Table 2. Clinical characteristics of the 68 patients with primary cicatricial alopecia

Clinical characteristics	No. (%)
Subtype	
Lymphocytic type	15 (22.1)
Lichen planopilaris/frontal fibrosing alopecia	7 (10.3)
Central centrifugal cicatricial alopecia	5 (7.4)
Lupus erythematosus	3 (4.4)
Neutrophilic type	50 (73.5)
Folliculitis decalvans	27 (39.7)
Dissecting cellulitis	23 (33.8)
Unclassified type	3 (4.4)
Taking antibiotics (within 3 mo)	
Yes	26 (38.2)
No	42 (61.8)
Clinical sign (can be duplicated)	
Erythematous macule/patch	67 (98.5)
Scale and dandruff	38 (55.9)
Oozing or crust	26 (38.2)
Pustule/abscess	31 (45.6)
Hair tufting	23 (33.8)
Disease duration	
Within 3 mo	5 (7.4)
3 mo–1 yr	8 (11.8)
1 yr–3 yr	19 (27.9)
Over 3 yr	36 (52.9)

The results of scalp bacterial culture

In total, 182 bacterial cultures were performed, from which 175 bacterial strains were isolated. Although most cultures yielded a single predominant strain, 20 cultures contained 2 co-predominant strains. Seven cultures (3.8%) showed no bacterial growth (Table 3).

Of the 175 bacterial strains, 155 (88.6%) were gram-positive and 20 (11.4%) were gram-negative. The PCA samples predominantly yielded gram-positive bacteria (86.5%), similar to those of the controls (90.1%). Bacterial composition analysis of the control subgroups (HV, TE, AGA, and AA) revealed no significant differences in the prevalence of gram-positive and gram-negative strains (Supplementary Table 1).

1) Gram-positive strains

Among gram-positive isolates, *S. capitis* (37.7%) was the most prevalent, followed by *S. epidermidis* (26.9%), *S. aureus* (11.4%), *S. warneri* (4.0%), and *S. lugdunensis* (3.4%). Other less common isolates included *S. caprae* (1.1%), *S. haemolyticus* (1.1%), *S. saprophyticus*, *Cutibacterium acnes*, *Streptococcus mitis*, and *S. sanguinis* (each 0.6%). The control group primarily consisted of *S. capitis* (54.5%) and *S. epidermidis* (25.7%), whereas the PCA samples showed significantly higher numbers of *S. aureus* (24.3%) and *S. lugdunensis* (8.1%) but fewer *S. capitis* (14.9%) isolates (all, $p < 0.01$) than control

Table 3. Isolated bacterial strains cultured from the scalp in this study

Bacterial strains	No. (%)							
	Total (n=175)	Controls (n=101)	PCA (n=74)	p-value*	FDR-corrected p-value	NCA (n=55)	p-value†	FDR-corrected p-value
Gram-positive strains	155 (88.6)	91 (90.1)	64 (86.5)			46 (83.6)		
<i>S. capitis</i>	66 (37.7)	55 (54.5)	11 (14.9)	<0.001	<0.001‡	8 (14.5)	<0.001	<0.001‡
<i>S. epidermidis</i>	47 (26.9)	26 (25.7)	21 (28.4)	0.572	1.000	20 (36.4)	0.141	0.362
<i>S. aureus</i>	20 (11.4)	2 (2.0)	18 (24.3)	<0.001	<0.001	14 (25.5)	<0.001	<0.001
<i>S. warneri</i>	7 (4.0)	3 (3.0)	4 (5.4)	0.383	1.000	2 (3.6)	0.811	0.811
<i>S. lugdunensis</i>	6 (3.4)	0 (0.0)	6 (8.1)	0.003	0.058	1 (1.8)	0.171	0.362
<i>S. caprae</i>	2 (1.1)	0 (0.0)	2 (2.7)	0.090	1.000	0 (0.0)	-	-
<i>S. haemolyticus</i>	2 (1.1)	2 (2.0)	0 (0.0)	0.233	1.000	0 (0.0)	0.296	0.431
<i>S. hominis</i>	1 (0.6)	1 (1.0)	0 (0.0)	0.400	1.000	0 (0.0)	0.461	0.487
<i>S. saprophyticus</i>	1 (0.6)	0 (0.0)	1 (1.4)	0.232	1.000	1 (1.8)	0.171	0.362
<i>S. mitis</i>	1 (0.6)	1 (1.0)	0 (0.0)	0.400	1.000	0 (0.0)	0.461	0.487
<i>S. sanguinis</i>	1 (0.6)	1 (1.0)	0 (0.0)	0.400	1.000	0 (0.0)	0.461	0.487
<i>C. acnes</i>	1 (0.6)	0 (0.0)	1 (1.4)	0.232	1.000	0 (0.0)	-	-
Gram-negative strains	20 (11.4)	10 (9.9)	10 (13.5)			9 (16.4)		
<i>K. aerogenes</i>	5 (2.9)	1 (1.0)	5 (6.8)	0.051	1.000	5 (9.1)	0.036	0.136
<i>A. lwoffii</i>	4 (2.3)	4 (4.0)	0 (0.0)	0.025	0.507	0 (0.0)	0.036	0.136
<i>K. pneumoniae</i>	4 (2.3)	1 (1.0)	3 (4.1)	0.264	1.000	2 (3.6)	0.437	0.487
<i>Moraxella group</i>	2 (1.1)	2 (2.0)	0 (0.0)	0.531	1.000	0 (0.0)	0.157	0.362
<i>A. pittii</i>	1 (0.6)	0 (0.0)	1 (1.4)	0.305	1.000	1 (1.8)	0.271	0.431
<i>A. radioresistens</i>	1 (0.6)	1 (1.0)	0 (0.0)	0.305	1.000	0 (0.0)	0.317	0.431
<i>A. ursingii</i>	1 (0.6)	1 (1.0)	0 (0.0)	0.305	1.000	0 (0.0)	0.317	0.431
<i>C. koseri</i>	1 (0.6)	0 (0.0)	1 (1.4)	0.305	1.000	1 (1.8)	0.271	0.431

Comparisons were conducted using the χ^2 test.

PCA: primary cicatricial alopecia, FDR: false discovery rate, NCA: neutrophilic primary cicatricial alopecia.

*Comparison between controls and PCA; †Comparison between controls and NCA.

‡FDR correction was applied using the Benjamini-Hochberg method.

samples. The results remained consistent after FDR corrections. In the NCA group, the most frequent isolates were *S. epidermidis* (36.4%) and *S. aureus* (25.5%).

Strains such as *S. lugdunensis*, *S. caprae*, *S. saprophyticus*, and *C. acnes* were unique to PCA, whereas *S. haemolyticus*, *S. hominis*, *S. mitis*, and *S. sanguinis* were found exclusively in the controls.

2) Gram-negative strains

The predominant gram-negative bacteria were *Klebsiella aerogenes* (2.9%) and *K. pneumoniae* (2.3%), followed by *Acinetobacter lwoffii* (2.3%), *Moraxella* group (1.1%), *A. pittii* (0.6%), *A. ursingii* (0.6%), and *Citrobacter koseri* (0.6%). Gram-negative strains were more frequently isolated from PCA samples (13.5%) than from control samples (9.9%), with the highest incidence observed in NCA samples (16.4%).

In PCA samples, *Klebsiella* spp. were predominant, particularly in the neutrophilic type (7/9 isolates), with only one isolate identified in the lymphocytic type. In contrast, the non-inflammatory control scalps were dominated by *Acinetobacter* species, including 4 *A. lwoffii* and one isolate each of *A. ursingii*, *A. radioresistens*, *K. aerogenes*, *K. pneumoniae*, and *C. koseri*. Further analysis of bacterial colonization in the PCA groups revealed no significant differences in the isolated bacterial species between those with and those without a history of recent antibiotic use.

Antibiotic susceptibility of the bacterial isolates

1) Gram-positive strains

The highest antibiotic resistance rates among gram-positive bacteria were observed against benzylpenicillin (53.3%), followed by fusidic acid (39.2%), mupirocin (19.7%), erythromycin (19.2%), tetracycline (16.9%), clindamycin (14.1%), and oxacillin (13.8%). Resistance to benzylpenicillin (74.6% vs. 37.9%), fusidic acid (57.1% vs. 25.9%), erythromycin (30.2% vs. 11.4%), clindamycin (25.4% vs. 5.8%), oxacillin (20.6% vs. 9.0%), and telithromycin (12.7% vs. 1.2%) was significantly higher in patients with PCA than in controls, both before and after FDR correction. Although the resistance rates for mupirocin, tetracycline, trimethoprim (TMP)/sulfamethoxazole (SMX), ciprofloxacin, and gentamicin were higher in patients with PCA, these differences were not statistically significant (Table 4).

In contrast, all gram-positive isolates in both the PCA and control groups were sensitive to vancomycin, teicoplanin, tigecycline, quinupristin/dalfopristin, habekacin, nitrofurantoin, and rifampicin.

2) Gram-negative strains

Among gram-negative strains, ampicillin (AMP, 84.6%) showed the highest resistance rate, followed by cefazolin (54.5%), cefoxitin (54.5%), AMP/sulbactam (SUL) (40.0%), and aztreonam

(15.4%). In the PCA samples, AMP resistance was 100% (9/9), with cefazolin and cefoxitin showing 55.6% resistance, and AMP/SUL at 50%. The higher resistance to AMP and AMP/SUL in PCA samples was statistically significant compared to that in controls, both before and after FDR corrections. In contrast, all gram-negative isolates from both groups were sensitive to carbapenem, cefotaxime, gentamicin, TMP/SMX, amikacin, piperacillin (PIP)/tazobactam (TZB), tigecycline, ceftazidime, cefepime, levofloxacin, and ertapenem. Antibiotic susceptibility patterns of *Klebsiella* species were similar in both groups, with 44.4% (4/9) of the isolates showing resistance only to AMP, whereas the remaining 55.6% (5/9) exhibited resistance to AMP, cefazolin, AMP/SUL, and cefoxitin. None of the strains showed resistance to other antibiotics.

Antibiotic susceptibility of patients with NCA

In patients with NCA, AMP showed the highest resistance rate (100%), followed by benzylpenicillin (73.9%), cefazolin (62.5%), cefoxitin (62.5%), fusidic acid (56.5%), and AMP/SUL (55.6%). Moderate resistance was observed for erythromycin (37.0%), mupirocin (32.6%), clindamycin (30.4%), oxacillin (26.1%), and tetracycline (26.1%). Notably, 15% (3/20) of *S. aureus* isolates were oxacillin-resistant and classified as methicillin-resistant *S. aureus* (MRSA), all of which were from patients with NCA. Lower resistance rates were observed for aztreonam (11.1%), TMP/SMX (9.1%), ciprofloxacin (8.7%), and gentamicin (5.5%) (Fig. 2, Supplementary Table 2).

Among these, the resistances for AMP, benzylpenicillin, cefoxitin, fusidic acid, AMP/SUL, erythromycin, mupirocin, clindamycin, oxacillin, telithromycin, and TMP/SMX were statistically significant. In contrast, the resistance rate for aztreonam was significantly higher in the control group than in the NCA group.

However, all isolates from patients with NCA were sensitive to tigecycline, linezolid, teicoplanin, vancomycin, habekacin, nitrofurantoin, rifampicin, amikacin, ceftazidime, PIP/TZB, ertapenem, cefepime, and cefotaxime.

DISCUSSION

The scalp microbiota is essential for maintaining a healthy scalp, with its disruptions associated with inflammatory conditions such as PCA^{7,10}. Previous studies have suggested that bacterial involvement plays a critical role in the pathogenesis of PCA, particularly of the neutrophilic type. In FD, *S. aureus* colonized 80% (16/20) of the affected and non-lesional scalp areas but was absent in healthy controls (0/20), suggesting its role in PCA. *S. aureus* biofilm formation enhances persistence, immune evasion, and treatment resistance in PCA^{4,6}. Similarly, *C. acnes* forms biofilm-like clusters

Table 4. Antibiotic susceptibility of the isolated gram-positive and gram-negative strains

Antibiotics	No. of isolate (PCA/control)						
	Total	Sensitive	Intermediate	Resistant	Resistance rate (%)	p-value	FDR-corrected p-value
Gram-positive (n=155)							
Benzylpenicillin	150 (63/87)	69 (16/53)	1 (0/1)	80 (47/33)	53.3 (74.6/37.9)	<0.001	<0.001
Fusidic acid	148 (63/85)	88 (25/63)	2 (2/0)	58 (36/22)	39.2 (57.1/25.9)	<0.001	<0.001
Mupirocin	142 (57/85)	110 (40/70)	4 (2/2)	28 (15/13)	19.7 (26.3/15.3)	0.055	0.085
Erythromycin	151 (63/88)	118 (44/74)	4 (0/4)	29 (19/10)	19.2 (30.2/11.4)	0.001	0.003
Tetracycline	154 (63/91)	126 (50/76)	2 (1/1)	26 (12/14)	16.9 (19.0/15.4)	0.493	0.493
Clindamycin	149 (63/86)	125 (46/79)	3 (1/2)	21 (16/5)	14.1 (25.4/5.8)	0.002	0.004
Oxacillin	152 (63/89)	131 (50/81)	0 (0/0)	21 (13/8)	13.8 (20.6/9.0)	0.020	0.039
Telithromycin	148 (63/85)	134 (53/81)	5 (2/3)	9 (8/1)	6.1 (12.7/1.2)	0.001	0.003
TMP/SMX	152 (63/89)	145 (58/87)	0 (0/0)	7 (5/2)	4.6 (7.9/2.2)	0.067	0.095
Ciprofloxacin	149 (63/86)	139 (57/82)	4 (2/2)	6 (4/2)	4.0 (6.3/2.3)	0.162	0.212
Gentamicin	152 (63/89)	136 (51/85)	11 (8/3)	5 (4/1)	3.3 (6.3/1.1)	0.051	0.085
Linezolid	149 (63/86)	148 (63/85)	0 (0/0)	1 (0/1)	0.7 (0.0/1.2)	0.279	0.339
Vancomycin	153 (63/90)	153 (63/90)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Teicoplanin	151 (63/88)	146 (60/86)	5 (3/2)	0 (0/0)	0.0 (0.0/0.0)	-	-
Tigecycline	149 (62/87)	149 (62/87)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Q/D	148 (63/85)	148 (63/85)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Habekacin	148 (63/85)	148 (63/85)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Nitrofurantoin	148 (63/85)	148 (63/85)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Rifampicin	148 (63/85)	148 (63/85)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Gram-negative (n=20)							
Ampicillin	13 (9/4)	2 (0/2)	0 (0/0)	11 (9/2)	84.6 (100.0/50.0)	<0.001	<0.001
Cefazolin	11 (9/2)	5 (4/1)	0 (0/0)	6 (5/1)	54.5 (55.6/50.0)	0.431	0.458
Cefoxitin	11 (9/2)	5 (4/1)	0 (0/0)	6 (5/1)	54.5 (55.6/50.0)	0.431	0.458
AMP/SUL	15 (10/5)	9 (5/4)	0 (0/0)	6 (5/1)	40.0 (50.0/20.0)	<0.001	<0.001
Aztreonam	13 (10/3)	11 (9/2)	0 (0/0)	2 (1/1)	15.4 (10.0/33.3)	<0.001	<0.001
Carbapenem	17 (10/7)	17 (10/7)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Cefotaxime	16 (10/6)	16 (10/6)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Gentamicin	15 (10/5)	15 (10/5)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
TMP/SMX	15 (10/5)	15 (10/5)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Amikacin	15 (9/6)	15 (9/6)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
PIP/TZB	14 (10/4)	14 (10/4)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Tigecycline	13 (10/3)	13 (10/3)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Ceftazidime	13 (10/3)	13 (10/3)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Cefepime	13 (10/3)	13 (10/3)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Levofloxacin	13 (10/3)	13 (10/3)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-
Ertapenem	11 (9/2)	11 (9/2)	0 (0/0)	0 (0/0)	0.0 (0.0/0.0)	-	-

Comparisons were conducted using the χ^2 test.

PCA: primary cicatricial alopecia, FDR: false discovery rate, TMP/SMX: trimethoprim/sulfamethoxazole, Q/D: quinupristin/dalfopristin, AMP/SUL: ampicillin/sulbactam, PIP/TZB: piperacillin/tazobactam.

FDR correction was applied using the Benjamini-Hochberg method.

within follicles, promoting antimicrobial resistance and chronic inflammation^{4,11}. Additionally, bacterial colonization and superinfection may exacerbate NCA by triggering excessive immune responses. *S. aureus* and other gram-positive bacteria release toxins that stimulate proinflammatory cytokines, damaging follicular structures^{12,13}. Notably, *S. aureus* activates the NLRP3 inflammasome pathway, leading to interleukin-1 β secretion and sustained neutrophilic inflammation.

This is the first comparative study to examine bacterial colonization and antibacterial resistance in various types of alopecia in the Korean population, comparing PCA with non-inflammatory scalp conditions. Consistent with previous findings⁶, patients with PCA, especially those with FD and DC, showed significantly

higher *S. aureus* isolates, while non-inflammatory controls were dominated by coagulase-negative *staphylococci* (CoNS), such as *S. capitis* and *S. epidermidis*. *S. aureus* is a facultative pathogen that frequently colonizes inflamed areas, exacerbating conditions such as atopic dermatitis. In contrast, *S. epidermidis* and *S. capitis*, the major human skin commensals, are abundant on the lipid-rich scalp of healthy individuals^{14,15}. Additionally, certain bacterial strains were unique to each group: *S. lugdunensis* and *C. acnes* in PCA, and *S. hominis* and *S. sanguinis* in the control groups. *S. lugdunensis* is increasingly recognized as an emerging pathogen that has previously been linked to infections in the lower body and extremities^{16,18}. It resembles *S. aureus* in pathogenicity and may contribute to PCA-related inflammation. *S. hominis* and *S. sanguinis*

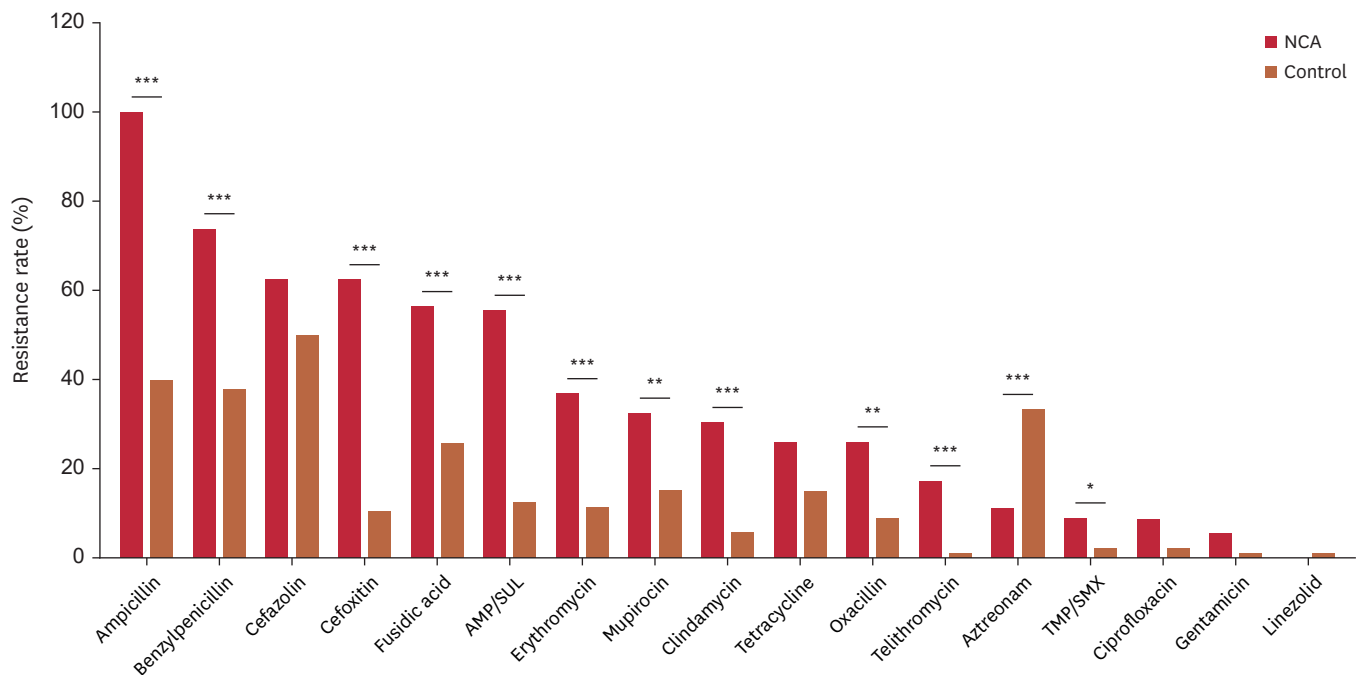


Fig. 2. Antibiotic resistance in patients with NCA and controls. Bar plot showing the percentage of antibiotic resistance in patients with NCA compared to the control groups. Significant differences were calculated using the χ^2 test. A false discovery rate correction was applied using the Benjamini-Hochberg method. NCA: neutrophilic primary cicatricial alopecia, AMP/SUL: ampicillin/sulbactam, TMP/SMX: trimethoprim/sulfamethoxazole.

* $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$.

are considered commensals that potentially play protective roles in maintaining scalp homeostasis. Given the beneficial effects of skin commensals in counteracting *S. aureus* colonization, further studies are required to explore their interactions within the PCA scalp microbiome and their potential protective roles.

Notably, gram-negative bacteria, particularly *Klebsiella* spp., were more prevalent in patients with PCA than in controls, with the highest incidence observed in patients with NCA. Consistently, a culture-based study of patients with FD found that 32% of infections were caused by gram-negative bacteria, including *Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella* spp., and *Pseudomonas aeruginosa*¹⁹. These findings broaden our understanding of non-staphylococcal dysbiosis in NCA and highlight the potential role of gram-negative bacteria in immune-mediated scalp inflammation.

Facultative gram-negative bacteria are increasingly recognized as causative agents of skin and soft tissue infections, particularly in individuals with compromised immune system, chronic wounds, or surgical site infections in hospital settings²⁰.

Alternatively, gram-negative folliculitis is considered a complication of long-term antibiotic use in patients with acne and rosacea. The overgrowth of gram-negative bacteria in patients with NCA may result from disruption of the microbial barrier, which consists of commensal flora (*C. acnes* and CoNS), following anti-staphylococcal antibiotic treatment^{6,19,21}. In contrast to

gram-positive pathogens, such as *S. aureus*, gram-negative bacteria frequently possess both intrinsic and acquired multi-drug resistance, complicating their treatment. Whether the gram-negative bacterial colonization of PCA is the primary cause of this condition or secondary overgrowth because of long-term antibiotic use remains unclear. Gram-negative bacteria, particularly *Klebsiella* spp., were more prevalent in patients with PCA than in controls, suggesting their potential role in disease exacerbation. *Klebsiella* spp. possess multiple virulence factors that enable immune evasion, including capsular polysaccharides that prevent complement-mediated lysis, lipopolysaccharides that activate toll-like receptor 4 and drive chronic inflammation, and siderophores that enhance iron acquisition for bacterial survival. Persistent immune activation in response to *Klebsiella* may contribute to sustained inflammation in patients with PCA.

It is also important to consider how the differences between lymphocytic and NCA may influence bacterial findings. Neutrophilic subtypes are associated with increased *S. aureus* and *Klebsiella* colonization, whereas lymphocytic subtypes, given their immune-mediated nature, may involve different bacterial contributions. Understanding these variations could offer deeper insights into microbial interactions.

PCA treatment varies according to the histological subtype, with immunosuppressants for the lymphocytic type and retinoids

or antimicrobials for the neutrophilic type^{21,22}. Commonly used antibiotics to reduce the bacterial load include oral doxycycline, cephalexin, clindamycin (alone or in combination with rifampicin), and topical mupirocin or fusidic acid. A retrospective study on FD demonstrated that oral tetracyclines and clindamycin–rifampicin combination were the most effective treatment regimens, with response rates of 90% and 100% over mean treatment durations of 4.6 and 7.2 months, respectively²³.

In this study, isolates from patients with PCA exhibited significantly higher resistance to benzylpenicillin (74.6%), fusidic acid (57.1%), erythromycin (30.2%), clindamycin (25.4%), and oxacillin (20.5%) than controls, suggesting increased resistance among scalp pathogens. The emergence of multi-drug-resistant strains is probably due to prolonged and widespread antibiotic use. These findings highlight the need for routine antibacterial susceptibility testing and alternative therapies, including new antibiotics. Gram-positive strains demonstrated resistance to several commonly used antibiotics, highlighting rifampicin, tetracycline, and vancomycin as alternative options for resistant cases. Gram-negative bacterial strains were highly resistant to cefazolin and AMP/SUL but remained susceptible to third- and fourth-generation cephalosporins and quinolones, which may be viable treatment options. Notably, MRSA was identified exclusively in patients with NCA, emphasizing the need for robust antibiotic stewardship and surveillance in this population. A recent study on bacterial skin infections in Korea similarly reported elevated resistance rates, with fusidic acid (36.2%), mupirocin (33.5%), oxacillin (22.3%), and clindamycin (20.2%) exhibiting reduced efficacy, and MRSA accounting for 22.7% of cases²⁴. Given these growing resistance trends, future research should prioritize optimizing treatment regimens based on antibacterial susceptibility results and exploring non-antibiotic-based therapeutic approaches for recalcitrant PCA cases.

This study has several limitations. First, its retrospective, single-center design introduces selection and data collection biases, limiting the ability to establish causal relationships and generalize its findings to broader populations. Second, confounding factors, including age, comorbidities, disease duration, and prior antibiotic exposure, may influence bacterial colonization and resistance profiles. The low prevalence of comorbidities minimizes confounding factors but may limit the detection of associations with scalp microbiota. The broad age range (5–75 years) introduces variability in immune function and microbial composition, whereas the disease duration, categorized into intervals, may affect colonization through chronic inflammation and antibiotic exposure. Although the differences were not statistically significant, prior antibiotic use in some patients with PCA may have influenced bacterial colonization and resistance patterns. These factors could introduce biases that were not fully accounted for in the adjusted

analyses, warranting further stratified investigations using larger sample sizes. Furthermore, the culture-based approach inherently limits the detection of the complete microbial community, particularly obligate anaerobes, such as *C. acnes*. Metagenomic sequencing can provide comprehensive insights into microbial diversity and functional genes associated with inflammation and antibiotic resistance, offering a more detailed characterization of microbial dynamics in PCA. Biofilm studies using confocal laser scanning microscopy and transcriptomics can elucidate virulence mechanisms in PCA chronicity. Additionally, single-cell RNA sequencing of immune cells in affected scalp regions may clarify host–microbe interactions and inflammatory pathways.

In conclusion, this study identified distinct bacterial colonization patterns and increased antimicrobial resistance in patients with PCA, especially in those with the neutrophilic subtypes. *S. aureus*, *S. lugdunensis*, and *Klebsiella* spp. were more prevalent in patients with PCA, linking bacterial superinfection to its pathogenesis. PCA isolates showed high resistance to first-line antibiotics used in dermatology, including mupirocin, clindamycin, oxacillin, and tetracycline, highlighting the need for routine bacterial culture and susceptibility testing to guide targeted therapies, particularly in recurrent or refractory NCA cases. Future studies integrating sequencing-based microbiome analyses and in vitro mechanistic investigations are warranted to elucidate microbial dynamics and their contribution to disease progression in PCA, with a focus on neutrophilic subtypes.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

DATA SHARING STATEMENT

The data supporting the findings of this study are available upon request from the corresponding authors. The data are not publicly available because of privacy and ethical restrictions.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Isolated bacterial strains cultured from the scalp in non-inflammatory healthy scalp controls

Supplementary Table 2

Antibiotic susceptibility of the isolated gram-positive and gram-negative strains between NCA and controls

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