

Alterations in the Hair Follicle Bacteriome and Mycobiome in Androgenetic Alopecia: A Cross-Sectional Study of 72 Patients and 24 Healthy Controls

Beibei Miao^{1,2,*}, Xueke Zou^{3,*}, Shuxia Yang⁴, Zixing Zhou⁵, Yuanyuan Geng^{1,2}, Shu Zhang^{1,2}, Jie Gong^{1,2,6}, Menglong Ran⁴

¹National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, People's Republic of China; ²National Institute for Communicable Disease Control and Prevention Joint Laboratory of Pathogenic Fungi, Peking University First Hospital, Beijing, People's Republic of China; ³Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, People's Republic of China; ⁴Department of Dermatology and Venereology, Peking University First Hospital; National Clinical Research Center for Skin and Sexually Transmitted Diseases; Key Laboratory of Molecular Diagnosis on Dermatoses; NMPA Key Laboratory for Quality Control and Evaluation of Cosmetics, Beijing, People's Republic of China; ⁵School of Public Health, Chengdu University of Traditional Chinese Medicine, Chengdu, Sichuan, People's Republic of China; ⁶Collaborative Innovation Center of Recovery and Reconstruction of Degraded Ecosystem in Wanjiang Basin Co-Founded by Anhui Province and Ministry of Education, School of Ecology and Environment, Anhui Normal University, Wuhu, Anhui, People's Republic of China

*These authors contributed equally to this work

Correspondence: Menglong Ran, Department of Dermatology and Venereology, Peking University First Hospital; National Clinical Research Center for Skin and Sexually Transmitted Diseases; Key Laboratory of Molecular Diagnosis on Dermatoses; NMPA Key Laboratory for Quality Control and Evaluation of Cosmetics, Beijing, People's Republic of China, Tel +86 10 83573273, Fax +86 10 83573103, Email rss-47@163.com

Purpose: Androgenetic alopecia (AGA) is characterized by perifollicular micro-inflammation, although its precise trigger remains elusive. Given that the hair follicle harbors a distinct microbiota which may modulate local immune responses, this study aimed to comprehensively profile the bacterial and fungal microbiome within the deep hair follicles of AGA patients versus healthy controls, and to evaluate the influence of disease severity, age, sex, and geographical environment.

Patients and Methods: We recruited 96 subjects (72 AGA patients and 24 healthy controls), collecting a total of 192 plucked hair follicle samples from the vertex and occipital scalp. Bacterial 16S rRNA (V3–V4) and fungal ITS regions were sequenced using the Illumina HiSeq platform. Bioinformatics pipelines were employed to analyze α - and β -diversity, as well as taxonomic composition, across multiple stratifications: disease stage, scalp region, age, sex, and geographical location.

Results: Bacterial community structure showed relative stability between groups. In contrast, fungal communities were markedly dysbiotic in AGA. A key finding was the significant depletion of the commensal yeast *Malassezia* in AGA follicles compared to controls ($p < 0.01$). Conversely, opportunistic taxa such as *Thermomyces* and *Bifidobacterium* were enriched in advanced disease stages. Notably, microbial α -diversity increased with both disease severity and age, indicating a disruption of the follicular niche (“niche collapse”). Male AGA patients exhibited distinct fungal shifts compared to females, and geographical location significantly shaped the follicular microbiome in patients but not in healthy controls.

Conclusion: Androgenetic alopecia involves fungal dysbiosis with loss of commensal *Malassezia* and gain of opportunistic microbes. Driven by host and environmental factors, this reframes AGA as an ecological imbalance, opening avenues for microbiome-targeted therapies.

Keywords: androgenetic alopecia, hair follicle, microbiome, *Malassezia*, micro-inflammation, dysbiosis

Introduction

Androgenetic alopecia (AGA) is the most common hair loss disorder globally, significantly impacting patients' psychological well-being and quality of life.^{1,2} While the primary pathogenesis involves the androgen-dependent miniaturization



of hair follicles in genetically predisposed individuals, recent evidence suggests that perifollicular micro-inflammation plays a crucial role in disease progression.^{3,4} Histological studies frequently reveal lymphocytic infiltration and fibrosis around the superior portion of the hair follicle in AGA, termed “micro-inflammation”.^{4,5}

The human hair follicle represents a unique ecological niche—humid, lipid-rich, and immune-privileged—distinct from the scalp surface.^{6–8} Commensal microbes residing in this niche interact with the host immune system. Dysbiosis (microbial imbalance) has been implicated in various inflammatory skin conditions, such as seborrheic dermatitis and acne.^{9,10} However, research on the AGA microbiome is limited, often focusing solely on bacteria or surface swabs, which may not reflect the deep follicular microenvironment.^{11–13}

Current literature regarding the role of fungi (the mycobiome) in AGA is sparse. More importantly, microbes within the hair follicle do not exist in isolation. Bacteria and fungi engage in complex inter-kingdom interactions, such as metabolic cross-feeding and the formation of mixed biofilms, which are crucial for maintaining skin homeostasis.^{13,14} In the lipid-rich niche of the hair follicle, lipophilic fungi like *Malassezia* and predominant bacteria like *Cutibacterium* synergistically metabolize sebum into free fatty acids. This co-metabolism can drive perifollicular micro-inflammation, a recognized exacerbating factor in AGA pathogenesis.^{15–17} Therefore, analyzing a single microbial kingdom fails to capture the intricate inter-kingdom network dynamics and their combined pathological potential. To fill this gap, this study conducts a large-scale, simultaneous dual-kingdom (bacterial and fungal) analysis of the hair follicle microbiome in Chinese subjects, investigating correlations with disease stage, age, sex, and environmental factors to elucidate the holistic ecological dysbiosis underlying AGA.

Materials and Methods

Subject Recruitment and Sample Collection

This cross-sectional study was approved by the Ethics Committee of Peking University First Hospital (No. 2021182). A total of 96 subjects were recruited, including 72 patients diagnosed with AGA (based on BASP classification and trichoscopy) and 24 healthy controls. Patients were clinically diagnosed according to the Basic and Specific (BASP) classification system, with trichoscopic confirmation (hair diameter diversity >20%, increased vellus hairs, reduced hair count per follicular unit). Healthy controls exhibited no clinical or trichoscopic signs of hair loss. Exclusion criteria for all participants comprised: (1) severe systemic diseases; (2) coexisting scalp disorders (eg, seborrheic dermatitis, psoriasis, folliculitis decalvans, alopecia areata, scarring alopecias) that could alter the scalp microbiome; (3) history of any AGA-directed therapies (ie, all enrolled AGA patients were strictly treatment-naive); (4) use of oral antibiotics or immunosuppressants within the past 1 month; (5) use of oral antifungal medications within the past 3 months; (6) application of topical scalp antifungals or antibacterial agents (including shampoos containing antifungal ingredients or zinc pyrithione) within the past 1 month; and (7) unwillingness to consent.

To standardize baseline conditions, subjects were instructed to abstain from hair washing and the application of any scalp treatments or hair care products for exactly 24 hours prior to sampling. Comprehensive clinical data were collected via a standardized clinical case report form. It should be noted that we did not directly measure sebum quantity or composition in this study.

Hair follicles were collected from two sites: the vertex (intersection of the median sagittal line and the coronal line connecting the tips of the ears) and the occipital region (below the external occipital protuberance). At each site, at least 10 hairs were plucked from an area of approximately 10 cm² using a sterile hemostat, resulting in a total of at least 20 hair follicles per participant. The hair roots containing follicular components were immediately cut with sterile scissors into sterile tubes containing 400 µL of 1X PBS and stored at –20°C or –80°C for subsequent DNA extraction. Although a formal a priori power analysis is challenging for microbiome studies due to unknown taxonomic effect sizes, our sample size (72 AGA patients and 24 healthy controls) was justified based on standard practices in human microbiome research and comparable prior studies, which indicate that >20 subjects per group provides sufficient power to detect significant community-level differences.

DNA Extraction and Sequencing

Samples were thawed, homogenized with zirconia beads after centrifugation, and incubated with lysis buffer and Proteinase K. Genomic DNA was extracted using a magnetic bead-based kit (Xi'an Tianlong). The extracted DNA was quantified, and the template DNA concentration was adjusted to approximately 20 ng/μL for subsequent PCR amplification. The V3–V4 region of the bacterial 16S rRNA gene (primers 341F/806R) and the fungal ITS1 region (primers ITS-1F/ITS1-R) were amplified using 8 μL of the DNA template in a 20 μL reaction volume. Sequencing libraries were generated and sequenced on an Illumina HiSeq platform (Illumina, San Diego, USA).

Bioinformatics and Statistical Analysis

Raw reads were merged (FLASH v1.2.7), filtered (Trimmomatic v0.39), and chimera-removed (UCHIME v4.2). In total, 109,148,404 reads were generated across all samples. Specifically, for the 16S rRNA sequencing, a total of 62,183,075 reads were obtained (averaging 323,870 reads per sample). For the ITS sequencing, a total of 46,965,329 reads were obtained (averaging 244,611 reads per sample). Following rigorous chimera removal, Operational Taxonomic Units (OTUs) were clustered at 97% similarity (QIIME2 v2021.11.0, UCLUST). While Amplicon Sequence Variant (ASV) methods provide higher resolution, the classic 97% OTU clustering was specifically retained in this study. This approach is highly robust for capturing broad, macroscopic community-level ecological shifts and is particularly well-suited for accommodating the massive natural length polymorphism inherent to the fungal ITS region, which can otherwise confound precise sequence variant algorithms. Taxonomy was assigned using the SILVA 138 (<http://www.arb-silva.de/>) (bacteria) and UNITE v8.2 (fungi) databases. Microbial diversity was calculated by α -diversity (Chao1, Shannon) and β -diversity (Bray-Curtis, UniFrac). Statistical analyses were performed using SPSS v26.0. Differences were analyzed using Wilcoxon rank-sum tests (two groups) or Kruskal–Wallis tests (multiple groups). LefSe (Linear Discriminant Analysis Effect Size) was used to identify biomarkers (LDA score > 2.0). $p < 0.05$ was considered statistically significant.

Results

Demographics and Sequencing Data

This study enrolled 96 participants, with a mean age of approximately 40 years (demographic details in Table 1; group composition in Table 2). High-throughput sequencing generated high-quality data, as confirmed by rarefaction curves indicating sufficient sequencing depth (Supplementary Figure 1).

Analysis of the microbial composition revealed consistent patterns across groups. The bacterial community was predominantly composed of the phyla Firmicutes, Proteobacteria, Bacteroidetes, and Actinobacteria (Supplementary Figure 2a), with detailed profiles provided in Supplementary Figure 2b–e. The fungal community was primarily dominated by Ascomycota and Basidiomycota (combined relative abundance >50% in all groups; Supplementary Figure 3a). At the class

Table 1 Demographic and Clinical Characteristics of the Study Population

Characteristics	AGA Group (n=72)	Healthy Control Group (n=24)
Specimen Collection, n (%)		
Total Samples	144	48
Vertex (Top) Region	72 (100%)	24 (100%)
Occipital Region	72 (100%)	24 (100%)
Disease Severity, n (%)		
Early AGA	39 (54.2%)	—
Typical/Advanced AGA	33 (45.8%)	—
Healthy	—	24 (100%)

(Continued)

Table 1 (Continued).

Characteristics	AGA Group (n=72)	Healthy Control Group (n=24)
Age (years)		
Mean \pm SD	40.17 \pm 14.83	40.21 \pm 18.41
18–29 years, n (%)	25 (34.7%)	7 (29.2%)
30–39 years, n (%)	14 (19.4%)	10 (41.7%)
\geq 40 years, n (%)	33 (45.8%)	7 (29.2%)
Sex, n (%)		
Male	37 (51.4%)	14 (58.3%)
Female	35 (48.6%)	10 (41.7%)
Geographical Location, n (%)		
Beijing	33 (45.8%)	6 (25.0%)
Shandong	39 (54.2%)	18 (75.0%)

Notes: Data are presented as number (percentage) for categorical variables and mean \pm standard deviation (SD) for continuous variables. The "Total Samples" represents the sum of samples collected from both the vertex and occipital regions for each participant.

Abbreviations: AGA, androgenetic alopecia; SD, standard deviation.

Table 2 Overview of Sample Groupings for Microbiome Analysis

Study Dimension	Grouping Purpose	Group Designation (Abbreviation)
Basic Grouping (Based on disease status and scalp region)	To compare baseline differences between alopecic and non-alopecic areas, and between AGA patients and healthy controls.	AGA Group: Vertex (TA), Occipital (OA) Control Group: Vertex (TC), Occipital (OC)
Disease Progression (Based on AGA stage)	To analyze microbiome variations across different stages of disease progression (early vs. typical).	Early AGA: Vertex (TEA), Occipital (OEA) Typical AGA: Vertex (TTA), Occipital (OTA) Control Group: Vertex (TC), Occipital (OC)
Age Factor (Based on age cohort)	To investigate the relationship between age and the follicular microbiome in AGA.	AGA Group: 18–29 years (A20), 30–39 years (A30), \geq 40 years (A40) Control Group: 18–29 years (C20), 30–39 years (C30), \geq 40 years (C40)
Sex Factor (Based on sex)	To analyze the influence of sex on the scalp microbiome in AGA.	AGA Group: Male Vertex (TMA), Male Occipital (OMA), Female Vertex (TFA), Female Occipital (OFA) Control Group: Male Vertex (TMC), Male Occipital (OMC), Female Vertex (TFC), Female Occipital (OFC)
Geographical Factor (Based on residence)	To compare potential effects of geographical region (Beijing vs. Shandong) on the microbiome.	AGA Group (Beijing): Vertex (TAB), Occipital (OAB) AGA Group (Shandong): Vertex (TAS), Occipital (OAS) Control Group (Beijing): Vertex (TCB), Occipital (OCB) Control Group (Shandong): Vertex (TCS), Occipital (OCS)

Abbreviations: AGA, androgenetic alopecia; TA/OA, top/occipital alopecia; TC/OC, top/occipital control; TEA/OEA, top/occipital early alopecia; TTA/OTA, top/occipital typical alopecia; A20/A30/A40, AGA group aged 18–29/30–39/ \geq 40 years; C20/C30/C40, control group aged 18–29/30–39/ \geq 40 years; TMA/OMA, top/occipital male alopecia; TFA/OFA, top/occipital female alopecia.

level, Eurotiomycetes, Saccharomycetes, Sordariomycetes, Dothideomycetes, and Mucoromycetes were most abundant (Supplementary Figure 3b). Key fungal genera included *Candida*, *Thermoascus*, *Aspergillus*, *Thermomyces*, *Saccharomyces*, *Rhizopus*, and *Malassezia* (Supplementary Figure 3e).

Fungal Dysbiosis Characterizes the Androgenetic Alopecia Follicular Microenvironment

Comparative analysis of the scalp hair follicle microbiome revealed a distinct ecological pattern: bacterial communities demonstrated significantly higher richness and evenness than fungal communities (Figure 1). While bacterial α -diversity remained stable, showing no significant difference between AGA patients and healthy controls ($p > 0.05$; Figure 1a, Supplementary Figure 2 and Table 3), the fungal community composition underwent marked restructuring in AGA (Figure 1b, Supplementary Figure 3 and Table 3).

This fungal dysbiosis was characterized by a significant shift in dominant taxa. Notably, *Malassezia*, the predominant fungal genus in healthy hair follicles, was substantially depleted in the AGA group compared to controls ($p < 0.01$, as highlighted in

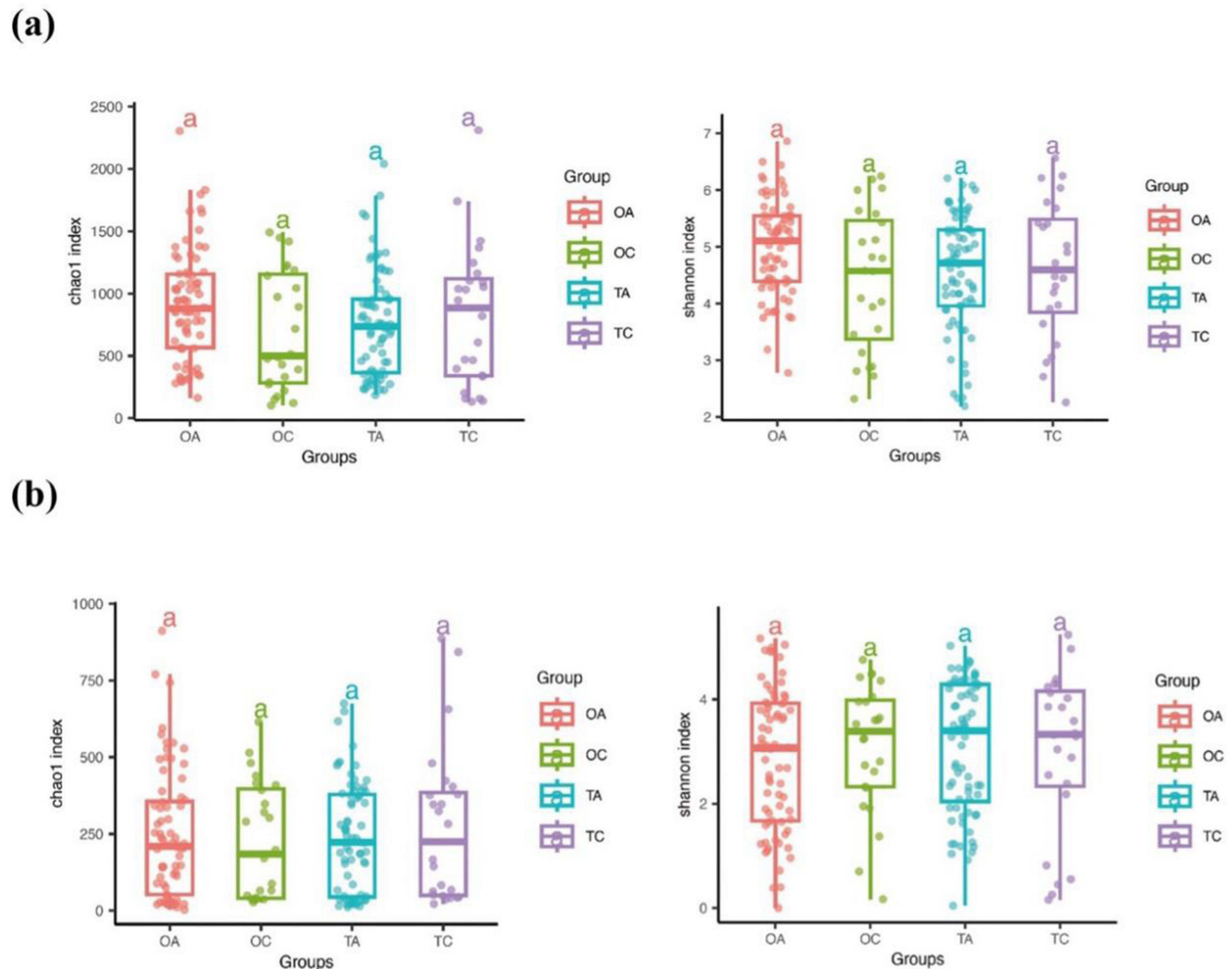


Figure 1 Baseline alpha diversity of bacterial and fungal communities shows no significant overall difference between AGA patients and healthy controls across scalp sites. (a) Bacterial alpha diversity (Chao1 and Shannon indices) exhibited no statistically significant differences among the four groups ($p > 0.05$). (b) Similarly, fungal alpha diversity remained unaltered across the groups ($p > 0.05$). Overall, the bacterial communities displayed higher richness and diversity compared to the fungal communities. Different lowercase letters (eg. a, b) above the boxes indicate statistically significant differences between groups ($p < 0.05$), whereas groups sharing at least one common letter (or identical letters) show no significant difference ($p > 0.05$).

Abbreviations: OA, occipital alopecia; OC, occipital control; TA, top alopecia; TC, top control.

Table 3). Its abundance did not differ between affected (vertex) and unaffected (occipital) sites within the same AGA patients. In contrast, the genus *Thermomyces* exhibited a site-specific enrichment, being significantly more abundant in the occipital region compared to the vertex in AGA patients ($p < 0.01$). Collectively, these data indicate that the onset of AGA is characterized not by a broad bacterial shift, but rather by a profound fungal dysbiosis driven primarily by the depletion of *Malassezia*.

Disease Progression is Associated with Elevated Microbial Diversity and Expansion of Opportunistic Taxa

Analysis of disease stage-stratified microbiome data revealed a correlation between AGA severity and microbial community changes. When comparing Early and Typical AGA stages, patients with Typical AGA exhibited a significant increase in bacterial α -diversity, as measured by the Shannon index (Figure 2a).

This progression was accompanied by significant shifts in specific microbial genera. The relative abundances of *Bifidobacterium*, *Corynebacterium*, *Saccharomycopsis*, and *Rhizopus* differed markedly between Early and Typical AGA stages ($p < 0.05$; Figure 2, bolded values in Table 4). Furthermore, the thermophilic fungus *Thermomyces* showed significant enrichment in severe alopecia areas. These results suggest that as AGA progresses, the miniaturizing follicle may lose its colonization resistance, transforming into a more permissive microenvironment that facilitates the influx and expansion of diverse, potentially opportunistic microbes.

Age-Dependent Shifts Define the AGA Follicular Microbiome

Our analysis identified patient age as a significant driver of microbial composition in AGA. When stratifying by age, older AGA patients (≥ 40 years) exhibited significantly higher α -diversity for both bacterial and fungal communities

Table 3 Mean Relative Abundance of Major Bacterial and Fungal Genera in Patients with Androgenetic Alopecia (AGA) and Healthy Controls

Bacterial/Fungal Genus	Mean Relative Abundance (%)				p - value			
	TA	OA	TC	OC	TA vs OA	TC vs OC	TA vs TC	OA vs OC
<i>Corynebacterium</i>	8.0%	4.68%	10.32%	18.45%	NS	NS	NS	NS
<i>Bacteroides</i>	6.29%	6.66%	5.68%	5.71%	NS	NS	NS	NS
<i>Staphylococcus</i>	4.43%	3.61%	7.19%	3.69%	NS	NS	NS	NS
<i>Ruminococcus</i>	1.87%	4.30%	4.12%	1.80%	NS	NS	NS	NS
<i>Faecalibacterium</i>	3.82%	2.79%	2.53%	1.86%	NS	NS	NS	NS
<i>Prevotella</i>	2.89%	3.96%	1.57%	1.52%	NS	NS	NS	NS
<i>Propionibacterium</i>	2.29%	2.88%	2.32%	4.68%	NS	NS	NS	NS
<i>Candida</i>	7.31%	7.04%	12.70%	11.38%	NS	NS	NS	NS
<i>Thermoascus</i>	5.56%	8.98%	3.37%	3.97%	NS	NS	NS	NS
<i>Aspergillus</i>	4.05%	3.58%	1.62%	2.13%	NS	NS	NS	NS
<i>Thermomyces</i>	2.77%	4.09%	1.83%	2.21%	$p < 0.05$	NS	NS	NS
<i>Saccharomycopsis</i>	3.72%	3.44%	0.39%	1.77%	NS	NS	NS	NS
<i>Rhizopus</i>	2.28%	3.17%	0.59%	1.55%	NS	NS	NS	NS
<i>Malassezia</i>	0.42%	1.24%	1.87%	9.48%	NS	NS	$p < 0.01$	$p < 0.01$

Notes: Data are presented as mean relative abundance (%). The genera *Corynebacterium* to *Propionibacterium* are bacteria, while *Candida*, *Thermoascus*, and *Aspergillus* are fungi. Bold values indicate statistical significance.

Abbreviations: AGA, androgenetic alopecia; TA, top alopecia; OA, occipital alopecia; TC, top control; OC, occipital control; NS, not significant ($p > 0.05$).

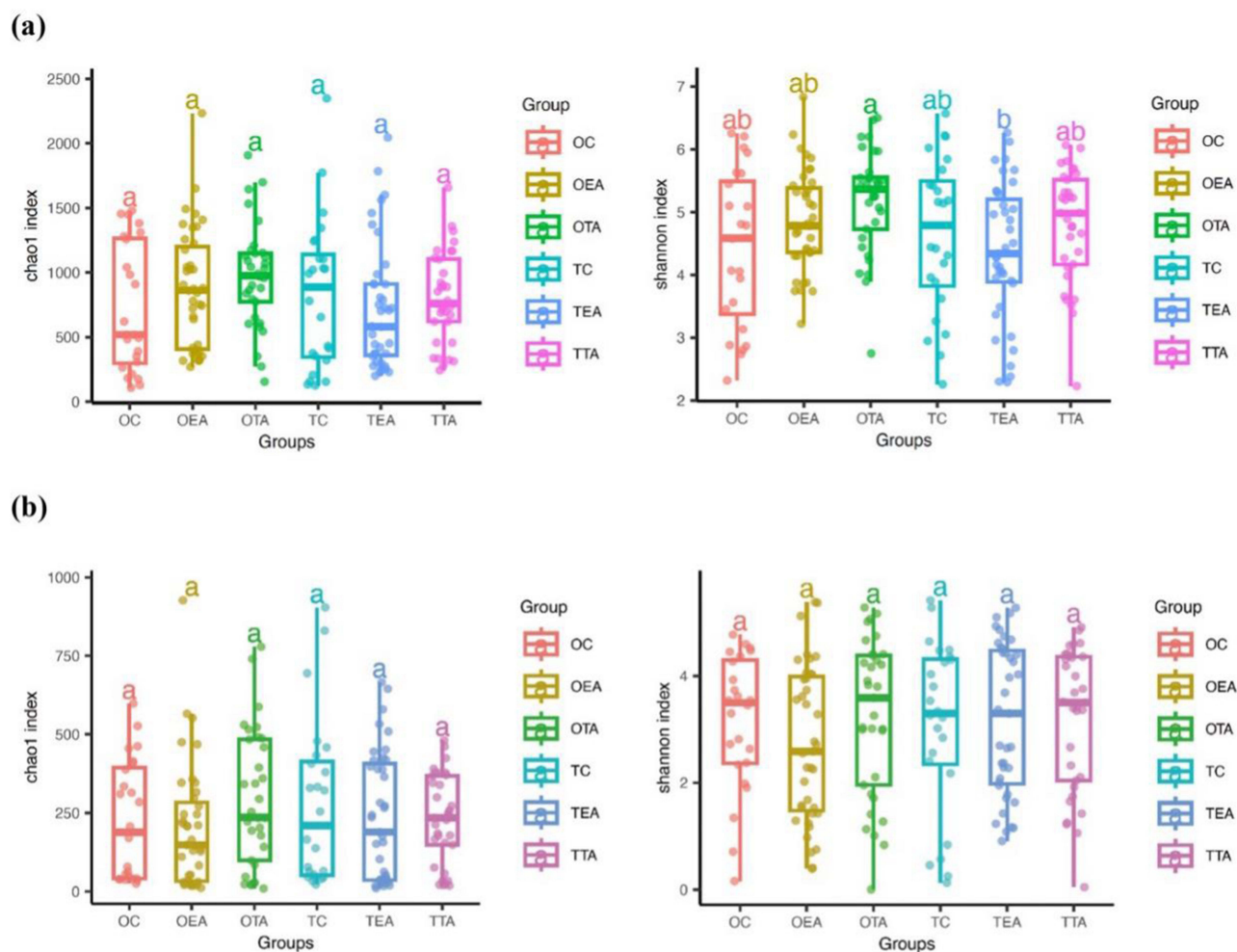


Figure 2 Disease progression (early vs. typical AGA) specifically alters bacterial, but not fungal, community diversity at distinct scalp sites. (a) For bacterial alpha diversity, while the Chao1 index showed no significant variation ($p > 0.05$), the Shannon index was significantly higher in the occipital typical alopecia (OTA) group compared to the top early alopecia (TEA) group ($p < 0.05$). (b) Fungal alpha diversity remained stable, with no significant differences in either index among the disease stage groups ($p > 0.05$). Different lowercase letters (eg, a, b) above the boxes indicate statistically significant differences between groups ($p < 0.05$), whereas groups sharing at least one common letter (eg, a and ab, or identical letters) show no significant difference ($p > 0.05$).

Abbreviations: OC, occipital control; OEA, occipital early alopecia; OTA, occipital typical alopecia; TC, top control; TEA, top early alopecia; TTA, top typical alopecia.

compared to the youngest group (18–29 years, $p < 0.05$) (Figures 3 and 4). Notably, the most pronounced dysbiosis was observed in the 30–39 age group, where the microbiome composition of AGA patients diverged most significantly from that of healthy controls. In contrast, the microbiomes of the youngest (18–29) and oldest (≥ 40) patient groups showed greater similarity to their respective healthy controls.

LEfSe analysis (LDA score > 2) further delineated age-specific taxonomic signatures (Supplementary Figures 4–7). In the bacterial community, the order Sphingomonadales was significantly enriched in young AGA patients, while the family Caulobacteraceae was prominent in older patients. Fungal communities also showed age-dependent patterns: the order Agaricales was significant in the 18–29 group, the class Dothideomycetes in the 30–39 group, and the class Mucoromycetes in the ≥ 40 group. Taken together, these data reveal that the follicular microbiome undergoes dynamic, age-specific restructuring, highlighting the fourth decade of life as a critical window for microbiome-associated disease progression in AGA.

Sex-Specific Microbial Signatures are Associated with AGA

Our analysis revealed distinct sexual dimorphism in the scalp microbiome of AGA patients (Figure 5 and Table 5). Crucially, these differences were specific to the disease state, as no significant sex-based variations were observed within the healthy control group.

Table 4 Mean Relative Abundance of Major Bacterial and Fungal Genera Across Different Disease Stages of Androgenetic Alopecia

Bacterial/Fungal Genus	Mean Relative Abundance (%)						p - value			
	TEA	OEA	TTA	OTA	TC	OC	TEA vs OEA	TTA vs OTA	TEA vs TTA vs TC	OEA vs OTA vs OC
<i>Corynebacterium</i>	14.33%	7.67%	0.51%	1.15%	10.32%	18.45%	NS	NS	NS	p<0.05
<i>Bacteroides</i>	6.03%	5.39%	6.59%	8.16%	5.68%	5.71%	NS	NS	NS	p<0.05
<i>Staphylococcus</i>	3.43%	2.44%	5.61%	4.99%	7.19%	3.69%	NS	NS	NS	NS
<i>Faecalibacterium</i>	3.11%	2.38%	4.66%	3.27%	2.53%	1.86%	NS	NS	NS	NS
<i>Prevotella</i>	2.20%	3.75%	3.71%	4.20%	1.57%	1.51%	NS	NS	NS	NS
<i>Propionibacterium</i>	1.83%	3.13%	2.83%	2.58%	2.32%	4.68%	NS	NS	NS	NS
<i>Bifidobacterium</i>	1.23%	2.37%	3.83%	4.65%	3.07%	1.92%	NS	NS	p<0.05	p<0.01
<i>Candida</i>	8.30%	8.95%	6.14%	4.78%	12.70%	11.37%	NS	NS	NS	NS
<i>Aspergillus</i>	4.82%	3.97%	3.13%	3.11%	1.62%	2.13%	NS	NS	NS	NS
<i>Saccharomycopsis</i>	1.89%	4.27%	5.87%	2.47%	0.39%	1.77%	NS	NS	p<0.05	NS
<i>Thermomyces</i>	2.23%	3.92%	3.41%	4.28%	1.83%	2.21%	NS	NS	NS	NS
<i>Rhizopus</i>	2.05%	3.10%	2.56%	3.26%	0.59%	1.55%	NS	NS	p<0.05	NS
<i>Thermoascus</i>	4.06%	8.32%	7.32%	9.76%	3.37%	3.97%	NS	NS	NS	NS
<i>Malassezia</i>	0.14%	0.71%	0.75%	1.86%	1.87%	9.48%	NS	NS	p<0.05	p<0.01

Notes: Data are presented as mean relative abundance (%). Statistical comparisons were performed between scalp sites within the same stage (TEA vs. OEA; TTA vs. OTA) and across different stages within the same site (Top: TEA vs. TTA vs. TC; Occipital: OEA vs. OTA vs. OC). Bold values indicate statistical significance.

Abbreviations: TEA, top early alopecia; OEA, occipital early alopecia; TTA, top typical alopecia; OTA, occipital typical alopecia; TC, top control; OC, occipital control; NS, not significant ($p > 0.05$).

In male AGA patients, bacterial α -diversity in the vertex (affected) region was significantly lower than in their own occipital (unaffected) region. Furthermore, comparative analysis between sexes showed that the vertex of male patients harbored significantly lower abundances of several fungal genera—including *Thermomyces*, *Thermoascus*, and *Rhizopus*—compared to the vertex of female patients ($p < 0.05$, key taxa highlighted in Table 5). In summary, these data demonstrate a distinct, sex-specific microbial dimorphism in AGA, where male affected follicles exhibit a more pronounced loss of microbial diversity and a distinct fungal profile compared to their female counterparts.

Environmental Factors Shape the Follicular Ecosystem

Our comparative analysis of subjects from two distinct geographic regions (Beijing vs. Shandong) reveals that the follicular microbiome is demonstrably shaped by external environmental factors, tightly linked to disease status.

While general α -diversity indices showed minimal significant differences (Figure 6), the structure of the microbial communities (β -diversity) exhibited marked geographical patterning. In healthy controls, bacterial and fungal community compositions showed no significant separation between geographical regions ($p > 0.05$, Supplementary Figures 8a, b, 9a and b), suggesting a resilient and selective follicular niche in the absence of disease.

In stark contrast, AGA patients displayed significant divergence in microbial community structure between the two locations ($p < 0.05$, Supplementary Figures 8c and 9b). Detailed compositional analysis (Table 6) confirmed significant, location-dependent shifts: the Beijing AGA cohort was enriched in *Corynebacterium* and *Staphylococcus*, whereas the Shandong AGA cohort showed higher abundances of *Bacteroides*, *Prevotella*, and *Saccharomycopsis* (all $p < 0.01$). LEfSe analysis further identified distinct microbial biomarkers strongly associated with each location (Supplementary Figures 10–13). Ultimately, these geographical comparisons reveal that while healthy follicles maintain a highly resilient

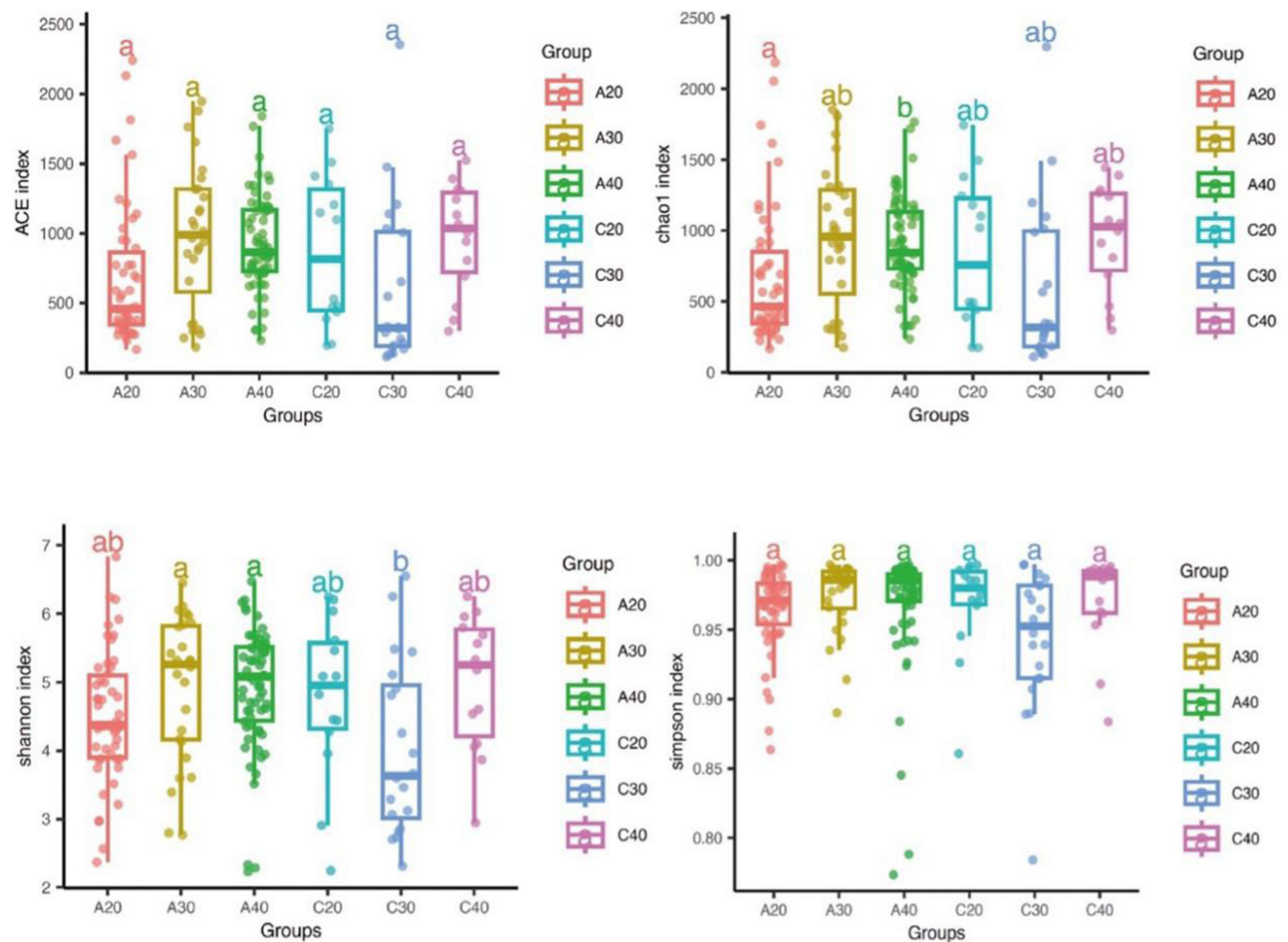


Figure 3 Bacterial microecological richness and diversity fluctuate significantly across different age stages in both AGA and healthy cohorts. Box plots display the ACE, Chao I, Shannon, and Simpson indices for bacterial communities. Different lowercase letters (eg, a, b) above the boxes indicate statistically significant differences between groups ($p < 0.05$), whereas groups sharing at least one common letter (eg, a and ab, or identical letters) show no significant difference ($p > 0.05$). The data demonstrate age-dependent variations in the scalp bacterial microbiome.

Abbreviations: A20, 18–29 in AGA group; A30, 30–39 in AGA group; A40, ≥ 40 in AGA group; C20, 18–29 in control group; C30, 30–39 in control group; C40, ≥ 40 in control group.

microbiome, the diseased AGA follicle loses its selective integrity, becoming a plastic niche highly susceptible to colonization by locally prevalent environmental microbes.

Discussion

The pathogenesis of AGA involves a complex interplay of genetic predisposition, androgen sensitivity, and follicular micro-inflammation.^{2,4} While the role of androgens is well-established, the trigger for the chronic perifollicular micro-inflammation remains elusive.³ Our study presents the largest dataset of the hair follicle microbiome in AGA to date, highlighting the crucial role of the mycobiome. Furthermore, our study provides the first comprehensive characterization of the deep follicular microbiome (both bacterial and fungal) in AGA, revealing that the disease is fundamentally an ecological disorder. Unlike superficial skin swabs, our deep-follicular sampling strategy uncovered a striking dichotomy: while bacterial communities remain relatively stable, the fungal mycobiome undergoes profound dysbiosis. The hallmark of this dysbiosis is the depletion of the commensal yeast *Malassezia* and the invasion of opportunistic non-resident taxa, driven by host factors such as age, sex, and environmental exposure. Our most striking finding is the depletion of *Malassezia* in AGA follicles. This observation challenges the conventional view of *Malassezia* in dermatology.¹⁸ *Malassezia* species, lipid-dependent yeasts that dominate the healthy scalp mycobiome, are conventionally linked to inflammatory conditions such as seborrheic dermatitis and dandruff when present in excess.^{19,20} However, our data

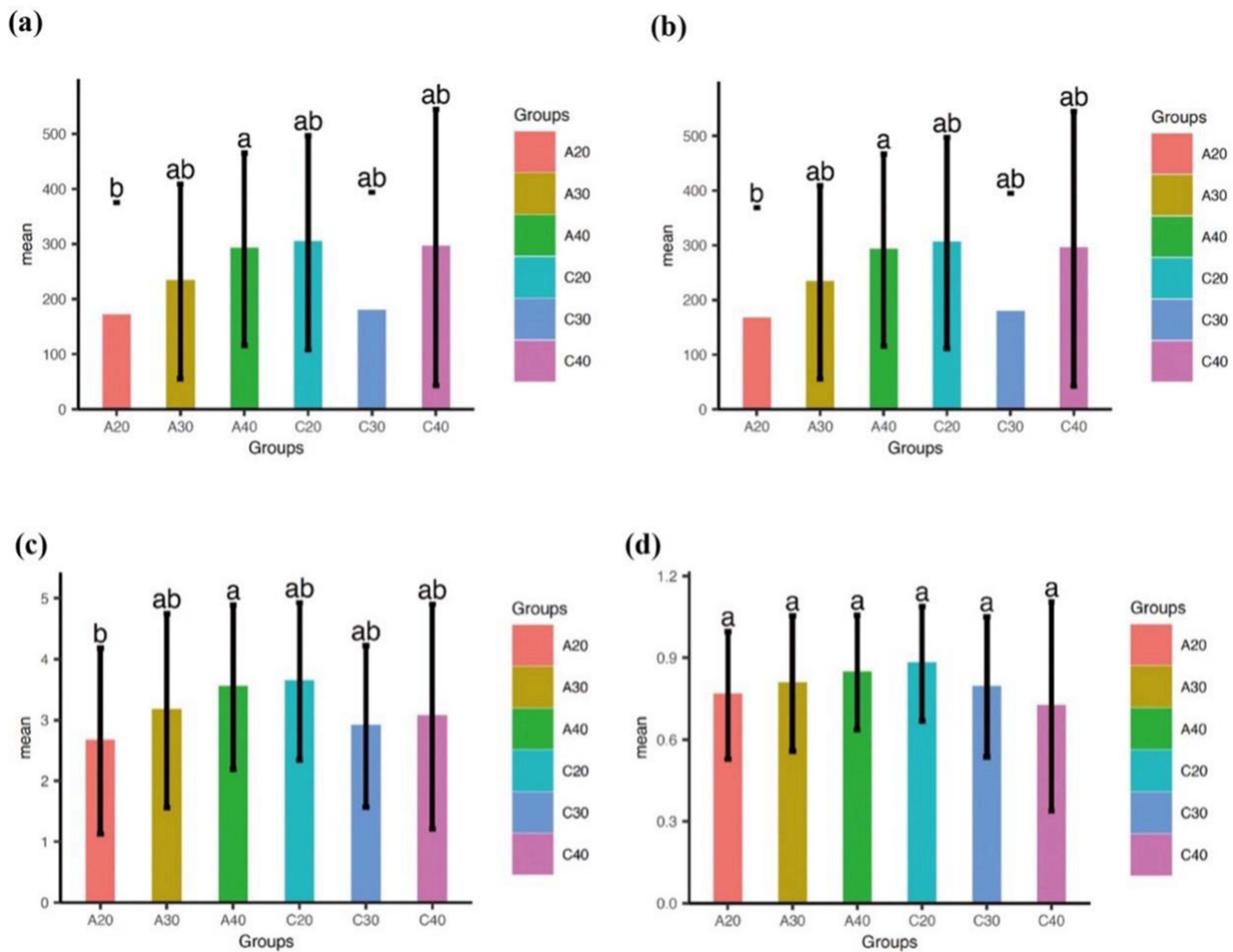


Figure 4 Age-related dynamics influence fungal community diversity, which exhibits lower overall richness compared to the bacterial microbiome. Fungal alpha diversity fluctuations between the AGA and control groups across the three age cohorts are shown utilizing (a) ACE, (b) Chao1, (c) Shannon, and (d) Simpson indices. Different lowercase letters above the bars indicate statistically significant differences ($p < 0.05$). Different lowercase letters (eg, a, b) above the bars indicate statistically significant differences between groups ($p < 0.05$), whereas groups sharing at least one common letter (eg, a and ab, or identical letters) show no significant difference ($p > 0.05$). **Abbreviations:** A20, 18–29 in AGA group; A30, 30–39 in AGA group; A40, ≥ 40 in AGA group; C20, 18–29 in control group; C30, 30–39 in control group; C40, ≥ 40 in control group.

indicate that within the deep follicular niche, *Malassezia* may serve as a keystone commensal organism essential for maintaining homeostasis. Through the hydrolysis of sebum, *Malassezia* releases free fatty acids that contribute to the cutaneous acid mantle, thereby helping to inhibit colonization by potential pathogens. In AGA, while the hair follicle undergoes progressive miniaturization, established histopathological evidence demonstrates that the attached sebaceous glands typically exhibit hypertrophy due to continuous androgenic (DHT) stimulation.^{21,22} Given that *Malassezia* is strictly a lipid-dependent yeast, its marked depletion in the presence of enlarged, active sebaceous glands presents a biological paradox. We hypothesize that this depletion is not driven by a quantitative lack of sebum, but rather by profound qualitative and structural changes within the follicular niche. First, under heightened androgen signaling, the precise lipidomic composition of the sebum (such as the specific ratios of squalene, triglycerides, and free fatty acids) may be fundamentally altered,²³ rendering the substrate biochemically unfavorable for commensal *Malassezia* strains. Second, the structural mismatch between a hypertrophied sebaceous gland and a drastically miniaturized hair shaft drastically alters the physical microanatomy of the follicular infundibulum.²⁴ This structural “niche collapse” likely leads to micro-comedone-like impaction, altered oxygen gradients, and the generation of localized oxidative stress. Consequently, this physically and biochemically transformed microenvironment becomes hostile to the resident *Malassezia*, stripping the follicle of the protective, immunomodulatory barrier provided by the yeast. The depletion of

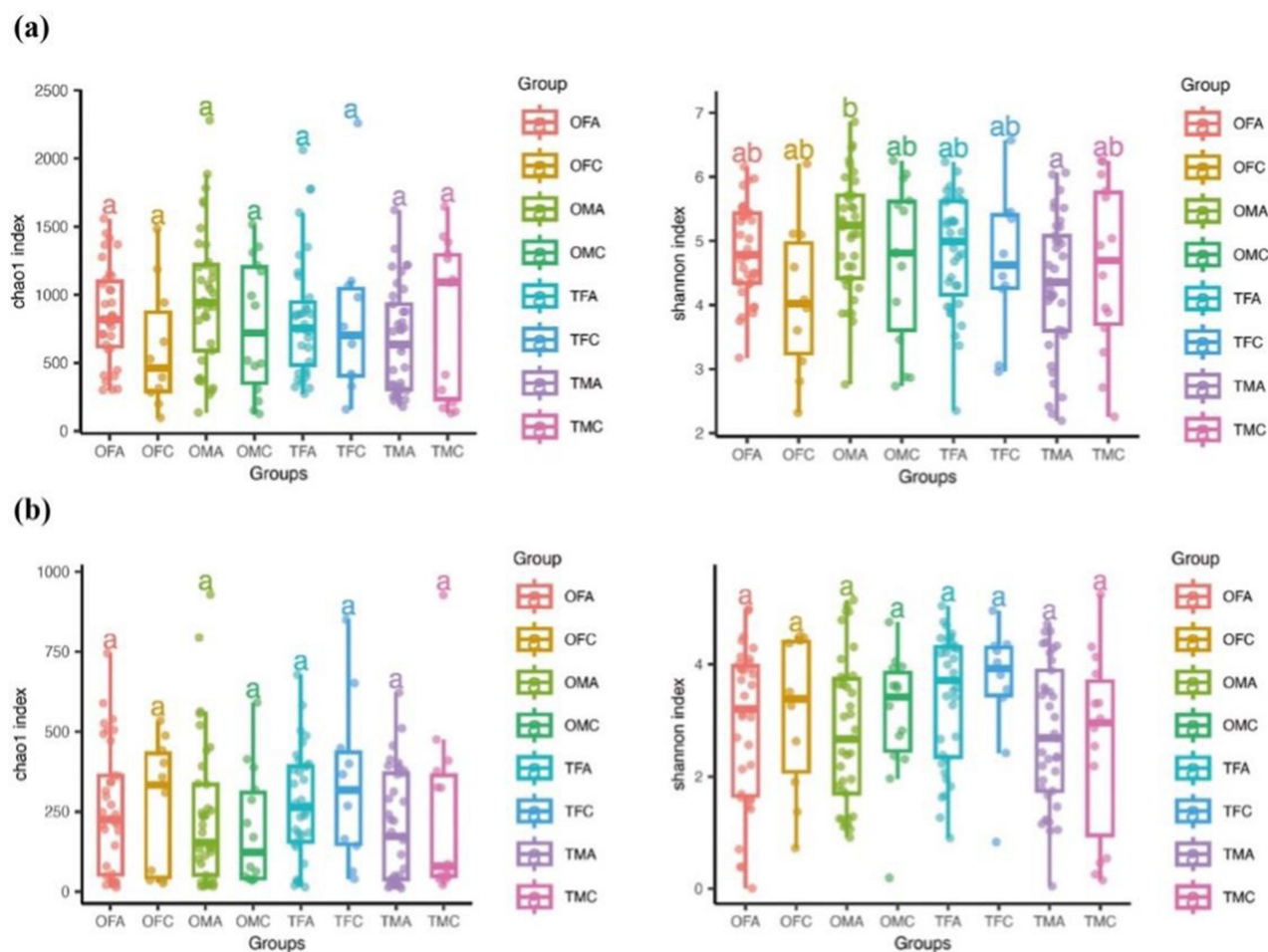


Figure 5 Gender significantly shapes the bacterial, but not the fungal, microecology of the scalp in AGA patients and controls. (a) Significant differences in bacterial alpha diversity were observed among groups based on gender and scalp site, as indicated by different lowercase letters ($p < 0.05$). (b) In contrast, the fungal community structure appeared highly stable, exhibiting no significant gender-driven variations ($p > 0.05$ for groups sharing the same letters). Different lowercase letters (eg, a, b) above the boxes indicate statistically significant differences between groups ($p < 0.05$), whereas groups sharing at least one common letter (eg, a and ab, or identical letters) show no significant difference ($p > 0.05$).

Abbreviations: OFA, occipital female alopecia; OFC, occipital female control; OMA, occipital male alopecia; OMC, occipital male control; TFA, top female alopecia; TFC, top female control; TMA, top male alopecia; TMC, top male control.

this keystone species thus vacates the ecological niche, creating a permissive environment that facilitates colonization by opportunistic microorganisms. We propose that under physiological conditions, *Malassezia* occupies the lipid-rich follicular niche, competitively excluding transient or pathogenic microbes through resource utilization and metabolite secretion. Its depletion in AGA may therefore vacate this ecological niche, leading to two principal consequences: first, the loss of immunomodulatory signals that *Malassezia* supplies to the follicular immune system; and second, the creation of a permissive environment that facilitates colonization by opportunistic microorganisms. The precise mechanism driving *Malassezia* depletion in AGA remains to be fully elucidated but likely relates to structural and biochemical changes in the follicular unit associated with miniaturization.

An intriguing observation in our study—and a common conundrum in AGA microbiome research—is the lack of significant microbial variation between the affected vertex and the clinically unaffected occipital region within AGA patients. This homogeneity strongly suggests that the observed mycobiome dysbiosis reflects a global, scalp-wide alteration driven by systemic host factors (such as overall androgenic tone affecting pan-scalp sebum properties) rather than a strictly localized pathology. Importantly, because our cohort was strictly treatment-naïve, this global shift cannot be attributed to prior therapeutic interventions. If the entire scalp shares a similar dysbiotic profile, why is hair miniaturization localized to the vertex? This apparent discrepancy can be explained by the well-established “regional

Table 5 Mean Relative Abundance of Major Bacterial and Fungal Genera Stratified by Sex and Scalp Site

Bacterial/ Fungal Genus	Mean Relative Abundance (%)								p - value							
	TMA	OMA	TFA	OFA	TMC	OMC	TFC	OFC	TMA vs OMA	TFA vs OFA	TMC vs OMC	TFC vs OFC	TMA vs TFA	TMC vs TFC	OMA vs OFA	OMC vs OFC
<i>Corynebacterium</i>	12.53%	2.88%	3.20%	6.59%	11.49%	14.99%	8.68%	23.28%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Bacteroides</i>	6.0%	6.72%	6.59%	6.59%	2.65%	6.44%	9.91%	4.68%	NS	NS	NS	NS	NS	p<0.05	NS	NS
<i>Staphylococcus</i>	7.16%	5.52%	1.55%	1.58%	8.23%	2.94%	5.74%	4.76%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Ruminococcus</i>	1.81%	4.04%	1.94%	4.57%	3.98%	1.83%	4.31%	1.75%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Faecalibacterium</i>	2.99%	2.52%	4.70%	3.07%	1.74%	2.21%	3.64%	1.38%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Prevotella</i>	1.99%	3.90%	3.84%	4.01%	1.30%	1.76%	1.96%	1.18%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Propionibacterium</i>	2.40%	4.44%	2.17%	1.23%	3.17%	7.50%	1.11%	0.73%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Candida</i>	10.25%	9.20%	4.20%	4.75%	11.01%	12.04%	15.07%	10.45%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Thermoascus</i>	4.06%	8.38%	7.14%	9.61%	4.98%	3.96%	1.11%	3.97%	NS	NS	NS	NS	p<0.05	NS	NS	NS
<i>Aspergillus</i>	4.44%	2.87%	3.64%	4.32%	1.76%	2.85%	1.42%	1.12%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Thermomyces</i>	1.71%	4.89%	3.89%	3.24%	2.69%	2.48%	0.64%	1.83%	p<0.05	NS	NS	NS	p<0.05	NS	NS	NS
<i>Saccharomycopsis</i>	2.52%	4.03%	4.98%	2.82%	0.54%	1.37%	0.17%	2.33%	NS	NS	NS	NS	p<0.05	NS	NS	NS
<i>Penicillium</i>	0.50%	0.52%	0.73%	0.80%	0.65%	7.55%	0.85%	0.81%	NS	NS	NS	NS	NS	NS	NS	NS
<i>Rhizopus</i>	2.19%	2.97%	2.38%	3.39%	0.69%	1.46%	0.45%	1.67%	NS	NS	NS	NS	p<0.05	NS	NS	NS

Notes: Data are presented as mean relative abundance (%). Statistical comparisons were performed to evaluate differences between scalp sites (Top vs. Occipital) within the same sex, and differences between sexes (Male vs. Female) within the same scalp site. Bold values indicate statistical significance.

Abbreviations: TMA/OMA, top/occipital male alopecia; TFA/OFA, top/occipital female alopecia; TMC/OMC, top/occipital male control; TFC/OFC, top/occipital female control; NS, not significant ($p > 0.05$).

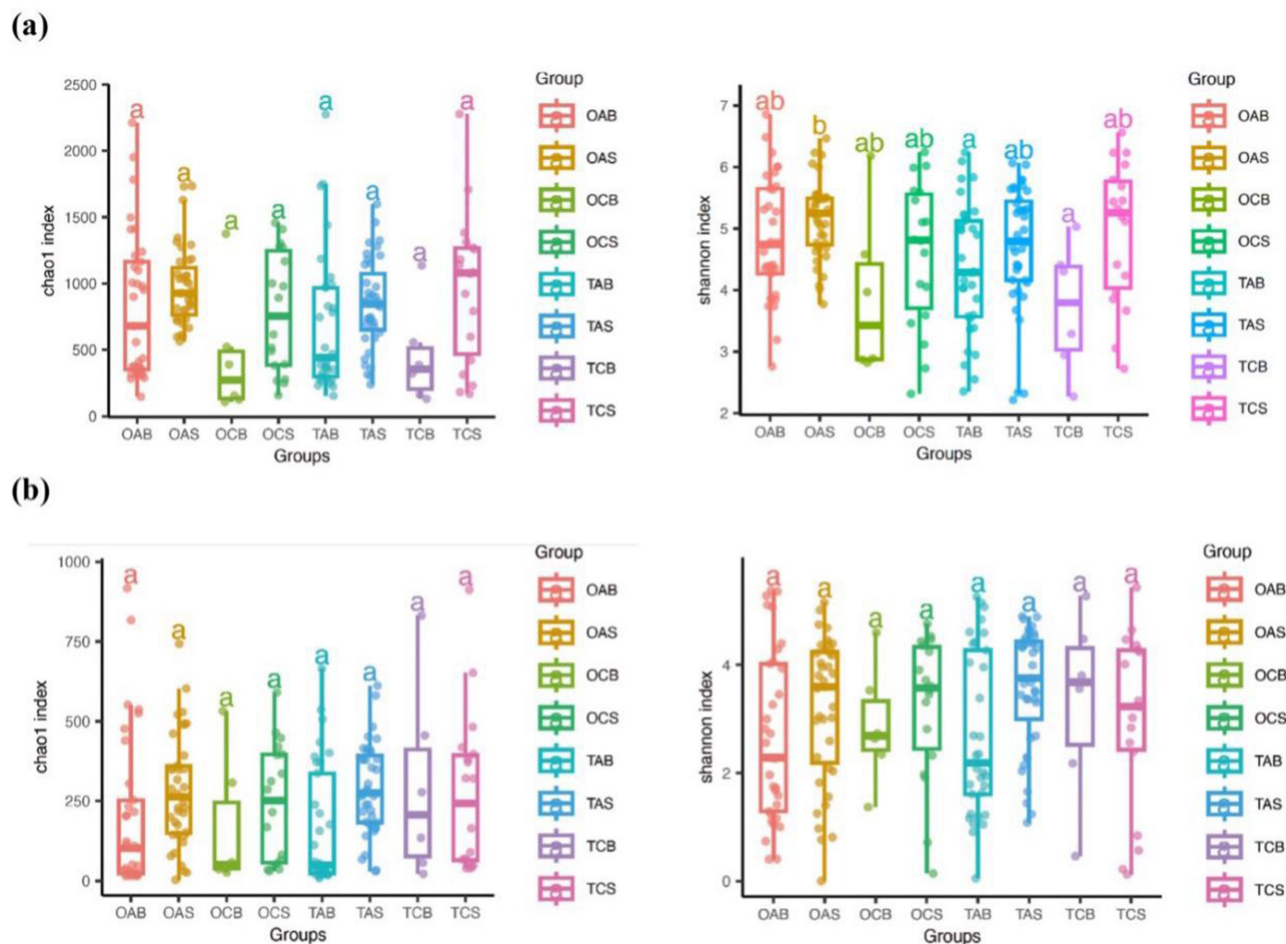


Figure 6 Geographical location (Beijing vs. Shandong) significantly influences both bacterial and fungal scalp microecology. (a) Box plots illustrate the distribution of bacterial Chao1 and Shannon indices, showing significant site- and city-specific variations (different lowercase letters denote $p < 0.05$). (b) For fungal communities, significant geographical variations were also observed, particularly in the Shannon index, indicating that residential location is a key driver of scalp fungal community evenness. Different lowercase letters (eg, a, b) above the boxes indicate statistically significant differences between groups ($p < 0.05$), whereas groups sharing at least one common letter (eg, a and ab, or identical letters) show no significant difference ($p > 0.05$).

Abbreviations: OAB, the occipital region of alopecia group in Beijing; OAS, the occipital region of alopecia group in Shandong; OCB, the occipital region of control group in Beijing; OCS, the occipital region of control group in Shandong; TAB, the top region of alopecia group in Beijing; TAS, the top region of alopecia group in Shandong; TCB, the top region of control group in Beijing; TCS, the top region of control group in Shandong.

specificity” of hair follicles. Vertex follicles are genetically programmed to exhibit higher androgen sensitivity (elevated 5- α reductase and androgen receptor expression) compared to occipital follicles. Consequently, we propose a synergistic “two-hit” model: while the entire scalp experiences microbial dysbiosis, the androgen-resistant occipital follicles can tolerate this altered microenvironment without undergoing miniaturization. In contrast, the genetically susceptible vertex follicles suffer from both androgen-driven structural changes and the subsequent micro-inflammation exacerbated by dysbiosis. Within this context, we hypothesize that the depletion of *Malassezia* is neither the primary initiating cause nor a mere epiphenomenon. Instead, it is likely a secondary consequence of early androgen-induced structural changes (niche collapse); however, the subsequent loss of its protective barrier function acts as a critical exacerbating factor, permitting opportunistic colonization that fuels a chronic pro-inflammatory feedback loop, thereby accelerating localized hair loss.

Paradoxically, we observed that microbial diversity increases with AGA severity. Contrary to the “high diversity equals health” paradigm often seen in gut microbiome studies,^{25–27} our results indicate that increased microbial α -diversity correlates with disease severity in AGA. We observed that patients with “Typical” (advanced) AGA exhibited significantly higher diversity than those in the “Early” stage. In the specific, semi-closed niche of the hair follicle, increased diversity likely represents “niche collapse” and the infiltration of transient, opportunistic microbes (eg,

Table 6 Mean Relative Abundance of Major Bacterial and Fungal Genera Stratified by Geographical Region (Beijing vs. Shandong)

Bacterial/ Fungal Genus	Mean Relative Abundance (%)								p - value							
	TAB	OAB	TAS	OAS	TCB	OCB	TCS	OCS	TAB vs OAB	TAS vs OAS	TCB vs OCB	TCS vs OCS	TAB vs TAS	OAB vs OAS	TCB vs TCS	OCB vs OCS
<i>Corynebacterium</i>	16.50%	8.37%	0.80%	1.56%	23.95%	36.86%	5.77%	12.31%	NS	NS	NS	NS	p<0.001	p<0.001	NS	NS
<i>Bacteroides</i>	3.65%	3.76%	8.51%	9.12%	9.29%	1.09%	4.48%	7.25%	NS	NS	NS	NS	p<0.001	p<0.001	NS	NS
<i>Staphylococcus</i>	9.0%	6.36%	0.56%	1.28%	6.41%	7.76%	7.45%	2.34%	NS	NS	NS	p<0.05	p<0.05	NS	NS	NS
<i>Faecalibacterium</i>	2.06%	1.96%	5.31%	3.49%	3.58%	0.49%	2.18%	2.32%	NS	NS	NS	NS	p<0.001	p<0.01	NS	NS
<i>Prevotella</i>	1.01%	2.10%	4.48%	5.52%	0.83%	0.91%	1.82%	1.72%	NS	NS	NS	NS	p<0.001	p<0.001	NS	NS
<i>Bifidobacterium</i>	0.86%	1.27%	3.74%	5.22%	3.36%	1.08%	2.97%	2.20%	NS	NS	NS	NS	p<0.001	p<0.001	NS	NS
<i>Propionibacterium</i>	3.07%	3.91%	1.62%	2.0%	0.23%	10.06%	3.01%	2.89%	NS	NS	p<0.05	NS	NS	p<0.01	NS	p<0.01
<i>Candida</i>	14.99%	9.89%	0.81%	4.62%	9.69%	19.52%	13.70%	8.67%	NS	NS	NS	NS	p<0.05	NS	NS	p<0.05
<i>Aspergillus</i>	3.93%	2.85%	4.15%	4.20%	1.49%	1.58%	1.66%	2.31%	NS	NS	NS	NS	p<0.01	p<0.05	NS	NS
<i>Saccharomycopsis</i>	0.47%	1.91%	6.47%	4.74%	0.09%	3.82%	0.48%	1.09%	NS	NS	NS	NS	p<0.001	p<0.01	NS	NS
<i>Thermomyces</i>	2.47%	4.13%	3.03%	4.05%	0.21%	1.86%	2.38%	2.32%	NS	NS	NS	NS	p<0.001	p<0.01	NS	NS
<i>Rhizopus</i>	0.57%	2.0%	3.74%	4.16%	0.35%	2.68%	0.67%	1.17%	NS	NS	NS	NS	p<0.001	p<0.01	NS	NS
<i>Thermoascus</i>	3.46%	6.88%	7.32%	10.76%	0.41%	4.37%	4.35%	3.83%	NS	NS	NS	NS	p<0.001	p<0.01	NS	NS
<i>Malassezia</i>	0.47%	1.99%	0.38%	0.60%	2.17%	10.39%	1.77%	9.17%	NS	NS	NS	NS	NS	NS	NS	NS

Notes: Data are presented as mean relative abundance (%). Statistical comparisons were performed to evaluate differences between scalp sites (Top vs Occipital) within the same geographical region, and differences between geographical regions (Beijing vs Shandong) within the same scalp site and disease group. Bold values indicate statistical significance.

Abbreviations: TAB/OAB, top/occipital alopecia group in Beijing; TAS/OAS, top/occipital alopecia group in Shandong; TCB/OCB, top/occipital control group in Beijing; TCS/OCS, top/occipital control group in Shandong; NS, not significant ($p > 0.05$).

Thermomyces, *Bifidobacterium*) due to a compromised barrier. The expansion of taxa such as *Bifidobacterium* and *Corynebacterium* suggests a shift towards a community structure that may perpetuate inflammation through distinct metabolic pathways. Furthermore, our spatial analysis revealed a particularly intriguing finding regarding *Thermomyces*, a known thermophilic (heat-loving) fungus. We observed that *Thermomyces* exhibited a striking site-specific enrichment in the occipital region compared to the vertex in AGA patients. To explain this spatial discrepancy, we propose a “thermodynamic microenvironment hypothesis.” The occipital region in AGA patients typically retains dense, healthy terminal hair, which acts as a highly effective thermal insulator, trapping body heat and creating a warmer, incubator-like micro-niche that specifically selects for thermophilic organisms. Conversely, the miniaturized or absent hair on the vertex leads to rapid heat dissipation and a cooler scalp surface. Addressing the question of its functional role, *Thermomyces* likely acts neither as a primary pathogen nor as a protective commensal, but rather as a temperature-driven opportunistic colonizer (an ecological bystander). Its enrichment in the occipital region is fundamentally a secondary consequence of the physical temperature gradient created by the pattern of hair preservation. Because the occipital follicles are genetically resistant to androgen-driven miniaturization, they tolerate the colonization of this thermophilic fungus without undergoing pathological hair loss.

Our stratification analysis highlights that the follicular microbiome is not static but dynamically evolves with host physiology. Host factors, particularly age and sex, were identified as key determinants of dysbiotic shifts. Notably, the 30–39 age group represented a critical period where the microbiome of AGA patients exhibited the most pronounced divergence from healthy controls. In younger patients (18–29), the enrichment of *Sphingomonas*—a genus known for its antioxidant sphingoglycolipids—may represent a compensatory protective mechanism against oxidative stress.^{28,29} The loss of such protective taxa in older groups, coupled with the expansion of *Caulobacteraceae* and *Mucoromycetes*, suggests that “microbial aging” parallels, and potentially accelerates, follicular aging. Furthermore, the observed sexual dimorphism provides novel insights into the clinical heterogeneity of AGA. Male patients exhibited lower microbial diversity and a more severe depletion of specific fungal taxa compared to females. This distinct “male follicular microbiome signature,” shaped by a potent androgenic environment exerting stronger selective pressure, may foster a more fragile ecological state that is less resilient to disturbance. This could, in part, explain the typically more rapid and severe progression of hair loss observed in males.

The geographical comparison between subjects from Beijing and Shandong lends strong support to the “Open Niche” hypothesis. While healthy follicles maintained a stable core microbiome across both regions, demonstrating ecological resilience and colonization resistance, AGA-affected follicles displayed significant geographical variation, with their microbial profiles mirroring the local environmental microbiota. This heightened plasticity indicates a loss of the follicle’s intrinsic capacity to filter exogenous microbial incursion. Consequently, regional environmental factors—such as pollutants, water quality, or climate—may differentially influence AGA progression by facilitating the colonization of location-specific opportunistic taxa into the compromised follicular niche.

From a clinical perspective, these ecological findings offer substantial translational opportunities and clinical relevance. First, the distinct microbial signatures identified in our study—particularly the depletion of *Malassezia* coupled with an increase in overall α -diversity and the infiltration of opportunistic taxa—could potentially serve as novel, non-invasive biomarkers. Monitoring these microbial shifts could aid dermatologists in evaluating disease severity, tracking progression, or assessing the efficacy of therapeutic interventions. Second, our findings challenge the traditional rationale for using broad-spectrum topical antimicrobials in AGA management, suggesting a paradigm shift toward microbiome-targeted ecological restoration. If *Malassezia* acts as a keystone commensal that maintains the acidic lipid mantle, therapeutic strategies could focus on repopulating the follicular niche with beneficial, commensal strains (probiotics) or supplementing the microenvironment with their favorable metabolites (postbiotics). Similarly, given the observed loss of protective taxa such as *Sphingomonas*, topical formulations incorporating specific prebiotics or antioxidant sphingolipids may help restore colonization resistance and mitigate perifollicular micro-inflammation. Finally, the significant variations in the microbiome driven by host age, sex, and geographical location strongly advocate for a personalized approach to adjuvant scalp care. Tailoring dermocosmetic treatments and topical therapies to a patient’s specific demographic and environmental context could improve the resilience of the follicular microbiome, thereby offering a more comprehensive, microenvironment-centric strategy for AGA management.

Several limitations of this study should be acknowledged. First, due to its cross-sectional design, causality cannot be established—whether microbial dysbiosis initiates follicular inflammation or arises as a consequence of an altered follicular microenvironment remains unclear. Second, although 16S and ITS sequencing offer broad taxonomic profiling, they do not capture functional activities; future metagenomic or metabolomic approaches are required to elucidate the metabolic impact of *Malassezia* depletion. Third, our cohort consisted exclusively of East Asian individuals, and the findings may not be generalizable to populations with different ethnic backgrounds, hair phenotypes, and sebum compositions. Fourth, while we comprehensively analyzed the follicular microbiome, we did not directly measure scalp sebum quantity or composition, which plays a crucial role in shaping the local microenvironment. Finally, as with any study involving the human skin microbiome, the routine use of daily scalp care products and shampoos represents a potential confounding factor. To minimize this, we strictly enrolled only treatment-naïve AGA patients (eliminating the confounding effects of prior AGA-directed therapies), excluded subjects who had recently used shampoos containing functional antimicrobial or antifungal agents (eg, zinc pyrithione), and enforced a standardized 24-hour unwashed baseline prior to sampling. Nevertheless, the long-term cumulative effects of cosmetic ingredients (such as surfactants and preservatives) in standard daily hair care products cannot be entirely ruled out. Future longitudinal studies integrating strictly controlled, standardized shampoo regimens, along with metabolomic and sebaceous profiling, are warranted to further isolate the disease-specific microbial shifts in the pathogenesis of AGA.

Conclusion

In conclusion, AGA is characterized by profound dysbiosis within the deep follicular microbiome, particularly within the fungal community. The hallmark of this imbalance is the depletion of the keystone commensal *Malassezia*, coupled with the infiltration of opportunistic taxa as disease severity increases. This microenvironment is dynamically shaped by host demographics and environmental factors, reflecting a critical loss of ecological resilience. Ultimately, our findings reframe AGA as a localized ecological disorder, highlighting microbiome-targeted modulation as a promising avenue for future therapeutic intervention.

Ethics and Consent

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to and the appropriate ethical review committee approval has been received. This study was approved by the Ethics Committee of Peking University First Hospital (No. 2021182) and conducted in accordance with the Declaration of Helsinki. Written informed consent for participation was obtained from all individual participants.

Acknowledgments

This work was supported by National Key Research and Development Program of China (Grant Number 2022YFC2504800), Strengthening Technical Capacity for Infectious Disease Surveillance and Control (Grant Number 102393240020020000003) and Major Project of Guangzhou National Laboratory (Grant Number GZNL2024A01025).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wang R, Lin J, Liu Q, Wu W, Wu J, Liu X. Micronutrients and androgenetic alopecia: a systematic review. *Mol Nutr Food Res*. 2024;68(22):e2400652. doi:10.1002/mnfr.202400652
2. Chen S, Zheng D, Wang H. Research progress on the pathogenesis of androgenetic alopecia. *Eur J Dermatol*. 2025;35(1):3–8. doi:10.1684/ejd.2025.4815
3. Mahé YF, Michelet JF, Billoni N, et al. Androgenetic alopecia and microinflammation. *Int J Dermatol*. 2000;39(8):576–584. doi:10.1046/j.1365-4362.2000.00612.x
4. Chen S, Li L, Ding W, Zhu Y, Zhou N. Androgenetic alopecia: an update on pathogenesis and pharmacological treatment. *Drug Des Devel Ther*. 2025;19:7349–7363. doi:10.2147/DDDT.S542000
5. Fields JR, Vonu PM, Monir RL, Schoch JJ. Topical ketoconazole for the treatment of androgenetic alopecia: a systematic review. *Dermatol Ther*. 2020;33(1):e13202. doi:10.1111/dth.13202

6. Lousada MB, Lachnit T, Edelkamp J, et al. Exploring the human hair follicle microbiome. *Br J Dermatol.* 2021;184(5):802–815. doi:10.1111/bjd.19461
7. Brinkac L, Clarke TH, Singh H, et al. Spatial and environmental variation of the human hair microbiota. *Sci Rep.* 2018;8(1):9017. doi:10.1038/s41598-018-27100-1
8. Zhang B, Chen T. Local and systemic mechanisms that control the hair follicle stem cell niche. *Nat Rev Mol Cell Biol.* 2024;25(2):87–100. doi:10.1038/s41580-023-00662-3
9. McCuaig B, Goto Y. Immunostimulating commensal bacteria and their potential use as therapeutics. *Int J Mol Sci.* 2023;24(21):15644.
10. Cha J, Kim T-G, Ryu J-H. Conversation between skin microbiota and the host: from early life to adulthood. *Exp Mol Med.* 2025;57(4):703–713. doi:10.1038/s12276-025-01427-y
11. Ho BS, Ho EXP, Chu CW, et al. Microbiome in the hair follicle of androgenetic alopecia patients. *PLoS One.* 2019;14(5):e0216330. doi:10.1371/journal.pone.0216330
12. Sharquie KE, Al-Obaidi HK. Onion juice (*Allium cepa* L.), a new topical treatment for alopecia areata. *J Dermatol.* 2002;29(6):343–346. doi:10.1111/j.1346-8138.2002.tb00277.x
13. Polak-Witka K, Rudnicka L, Blume-Peytavi U, Vogt A. The role of the microbiome in scalp hair follicle biology and disease. *Exp Dermatol.* 2020;29(3):286–294. doi:10.1111/exd.13935
14. Byrd AL, Belkaid Y, Segre JA. The human skin microbiome. *Nat Rev Microbiol.* 2018;16(3):143–155. doi:10.1038/nrmicro.2017.157
15. Suzuki K, Inoue M, Cho O, et al. Scalp microbiome and sebum composition in Japanese male individuals with and without androgenetic alopecia. *Microorganisms.* 2021;9(10). doi:10.3390/microorganisms9102132
16. Sugita T. [Skin microbiome and dermatitis: focusing on two distinct skin diseases, atopic dermatitis and Androgenetic alopecia]. *Yakugaku Zasshi.* 2025;145(8):689–695. Japanese doi:10.1248/yakushi.24-00190-5
17. Wang X, Li F, Sun Y, Meng F, Song Y, Su X. Microbial dysbiosis and its diagnostic potential in androgenetic alopecia: insights from multi-kingdom sequencing and machine learning. *mSystems.* 2025;10(6):e0054825. doi:10.1128/msystems.00548-25
18. Shah RR, Larrondo J, Dawson T, McMichael A. Scalp microbiome: a guide to better understanding scalp diseases and treatments. *Archiv Dermatological Res.* 2024;316(8):495. doi:10.1007/s00403-024-03235-2
19. Clark GW, Pope SM, Jaboori KA. Diagnosis and treatment of seborrheic dermatitis. *Am Fam Physician.* 2015;91(3):185–190.
20. Piacentini F, Camera E, Di Nardo A, Dell'Anna ML. Seborrheic dermatitis: exploring the complex interplay with *Malassezia*. *Int J Mol Sci.* 2025;26(6). doi:10.3390/ijms26062650
21. Whiting DA. Diagnostic and predictive value of horizontal sections of scalp biopsy specimens in male pattern androgenetic alopecia. *J Am Acad Dermatol.* 1993;28(5 Pt 1):755–763. doi:10.1016/0190-9622(93)70106-4
22. Sinclair R, Torkamani N, Jones L. Androgenetic alopecia: new insights into the pathogenesis and mechanism of hair loss. *F1000Res.* 2015;4:585. doi:10.12688/f1000research.6401.1
23. Schmidt M, Binder H, Schneider MR. The metabolic underpinnings of sebaceous lipogenesis. *Commun Biol.* 2025;8(1):670. doi:10.1038/s42003-025-08105-9
24. Mosca S, Ottaviani M, Briganti S, Di Nardo A, Flori E. The sebaceous gland: a key player in the balance between homeostasis and inflammatory skin diseases. *Cells.* 2025;14(10). doi:10.3390/cells14100747
25. Ross FC, Patangia D, Grimaud G, et al. The interplay between diet and the gut microbiome: implications for health and disease. *Nat Rev Microbiol.* 2024;22(11):671–686. doi:10.1038/s41579-024-01068-4
26. Huang G, Qu Q, Wang M, Huang M, Zhou W, Wei F. Global landscape of gut microbiome diversity and antibiotic resistomes across vertebrates. *Sci Total Environ.* 2022;838(Pt 2):156178. doi:10.1016/j.scitotenv.2022.156178
27. Varghese S, Rao S, Khattak A, Zamir F, Chaari A. Physical exercise and the gut microbiome: a bidirectional relationship influencing health and performance. *Nutrients.* 2024;16(21). doi:10.3390/nu16213663
28. Harel N, Ogen-Shtern N, Reshef L, Biran D, Ron EZ, Gophna U. Skin microbiome bacteria enriched following long sun exposure can reduce oxidative damage. *Res Microbiol.* 2023;174(8):104138. doi:10.1016/j.resmic.2023.104138
29. Wallace BA, Varona NS, Stiffler AK, Vermeij MJA, Silveira C. High microbial diversity, functional redundancy, and prophage enrichment support the success of the yellow pencil coral, *Madracis mirabilis*, in Curaçao's coral reefs. *mSystems.* 2025;10(11):e0120825. doi:10.1128/msystems.01208-25

Clinical, Cosmetic and Investigational Dermatology

Publish your work in this journal

Clinical, Cosmetic and Investigational Dermatology is an international, peer-reviewed, open access, online journal that focuses on the latest clinical and experimental research in all aspects of skin disease and cosmetic interventions. This journal is indexed on CAS. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/clinical-cosmetic-and-investigational-dermatology-journal>

Dovepress
Taylor & Francis Group