

Facial Physiological Characteristics and Skin Microbiomes Changes are Associated with Body Mass Index (BMI)

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Background: Overweight and obesity have become public health problems worldwide. An increasing number of research works are focusing on skin physiology and the manifestations of obesity-associated skin diseases, but little is known about the correlations between body mass index (BMI), facial skin physiological parameters, and the facial skin microbiome in healthy women.

Objective: To investigate the correlations between BMI, facial skin physiological parameters and facial bacteria and fungi in 198 women aged 18 to 35 years in Shanghai.

Methods: According to the international BMI standard and Chinese reference standard, subjects were divided into three groups, “lean” B1, “normal” B2 and “overweight” B3, and the physiological parameters of facial skin were measured by non-invasive instrumental methods, and the skin microbiota was analyzed by 16S rRNA and ITS high-throughput sequencing.

Results: Compared with the skin physiological parameters of the normal group, those of the overweight group exhibited a significant increase in trans-epidermal water loss (TEWL), which indicated that the skin barrier was impaired. The skin haemoglobin content was significantly increased, and skin surface pH was significant decreased in those with a high BMI. Furthermore, α -diversity, analysed using the Shannon, Chao, Sobs, and Ace indexes, was increased in the overweight group, suggesting that the diversity and species abundance of facial bacterial and fungal microbiota were also increased. Moreover, the overweight group had higher abundances of *Streptococcus*, *Corynebacterium*, *Malassezia*, and *Candida*. Notably, skin surface pH was significantly and negatively correlated with the relative abundances of *Malassezia*, *Candida*, and *Cladosporium*. Besides, the abundance of *Malassezia* was positively associated with the abundances of *Staphylococcus* and *Corynebacterium*.

Conclusion: These results indicate that BMI is associated with differences in the biophysical properties and microbiome of the facial skin. A high BMI affects the integrity of skin barrier and changes the skin flora diversity and species composition.

Keywords: body mass index, skin physiological parameters, microbiome, skin pH, *Corynebacterium*, *Malassezia*

Introduction

Body mass index (BMI) is an important indicator for monitoring physical health. The prevalence of obesity has increased worldwide in recent years, and overweight and obesity have become a significant public health problem.^{1,2} Multiple studies have confirmed that obesity causes many chronic diseases, including cardiovascular diseases, diabetes, liver diseases, and some cancers.^{3,4} Recent studies have provided evidence that obesity is a major risk factor for inflammatory skin diseases, including eczema, atopic dermatitis, psoriasis, and skin malignancies.⁵ Not only does obesity induce underlying diseases, seriously affecting life expectancy, but it also has a serious impact on mental health as well as the spiritual and social aspects of life.⁶

The skin is a multifunctional organ that acts as a physical, chemical, and immune barrier against the external environment.⁷ Many studies have revealed correlations between obesity and skin physiology. In the manifestations of obesity-associated skin diseases, some important skin parameters, such as sebum, skin stratum corneum hydration, trans-epidermal water loss (TEWL), skin surface pH, and elasticity, have been observed to undergo changes.^{4,8,9} Such previous studies have conclusively elucidated that obesity affects skin barrier, skin physiology and wound healing.⁴ In addition, sebum and sweat production increases, with higher incidences of acne and dermatoses, such as intertrigo.^{3,10} Obesity is also associated with microvascular dysfunction, chronic venous disease, and lymphedema and the increased incidence or aggravation of the symptoms of skin disorders.⁴

The skin is colonised by an assemblage of commensal microorganisms, including bacteria, fungi and viruses, that compose the skin microbiota.¹¹ Many research efforts have demonstrated that the skin microbiota plays a crucial role in maintaining skin homeostasis.¹² The diversity and abundance of species within the skin microbiota are easily influenced by both intrinsic factors and external factors.^{13,14} The intrinsic factors include the host's ethnicity, gender, age, individual physical condition, BMI, and different skin sites, while the external factors include climate, air quality, living environment, sleeping times, and personal hygiene habits, and so on.^{11,13,15–17}

BMI is an important intrinsic factor that influences physiological indices and the microbiome, and several studies have revealed a strong link between obesity and the human gut microbiome.^{18,19} Beyond the gut, attention has also been paid to the impact of BMI on the microbiota of other body sites. Multiple research studies have confirmed that BMI affects the species diversity and composition of site-specific microbial communities, such as those in the vagina, inguinal folds, vulva, abdomen, forearm, and shin.^{20–22}

The skin microbiome has been well-characterised and is known to harbour distinct site-specific microbial communities that are influenced by the biophysical properties of their niches, such as moisture levels, sebum, and skin surface pH.¹¹ However, little is known about the association between BMI and facial skin, especially the facial skin microbiome. In our current study, we aimed to investigate the correlations between BMI, facial skin properties, and the skin microbiome. The results will further our knowledge of microbiota–host interactions in the skin.

Materials and Methods

Volunteer Recruitment

This study was based on the investigation of the correlation between skin health status and the skin and gut microbiota of qualified volunteers living in Shanghai (aged 18–60, $n = 494$). Our research complied with the Declaration of Helsinki. Each subject was informed of the entire purpose and procedures of the research and signed an informed consent form before participating in the study. Volunteers had no skin diseases, had not taken or injected drugs (antibiotics, hormones, immunosuppressants, etc.) in the past 3 months, had not used any topical anti-inflammatory drugs on the test site (face) in the last 2 months prior to the study, had not undergone treatments for asthma or other chronic respiratory diseases, were not lactating or pregnant, and had not enrolled in other clinical trials. All volunteers were asked to carefully complete a self-evaluation questionnaire, which included questions about their skin condition, life habits and physiology. Ethical approval was provided by the Institutional Ethics Committee of Shanghai Jiao Tong University, Affiliated Sixth People's Hospital South Campus (Shanghai Fengxian District Central Hospital, Approval No.: 2021-KY-15). All skin parameters and microbial samples were collected in July 2021.

BMI Groups

The BMI (kg/m^2) of each subject was calculated from their weight (in kilograms) and height (in meters). Considering that the skin physiological parameters and skin microbiota are significantly influenced by gender, age, and skin site,^{13,23} data on the biophysical parameters and microbiota of the cheek from a total of 198 healthy women aged 18–35 years were included in this study. According to the international standard and Chinese reference standard for BMI.^{24,25} The recruited volunteers were divided into four groups: a lean group, $\text{BMI} < 18.5 \text{ kg}/\text{m}^2$; a normal group, $18.5 \text{ kg}/\text{m}^2 \leq \text{BMI} < 24 \text{ kg}/\text{m}^2$; an overweight group, $24 \text{ kg}/\text{m}^2 \leq \text{BMI} < 28 \text{ kg}/\text{m}^2$; and an obese group, $\text{BMI} \geq 28 \text{ kg}/\text{m}^2$. There was only one volunteer in the obese group, thus, to ensure the effectiveness of the statistical analysis, the obese group was excluded from this study. The

Table 1 Basic Information on the Participants in Each Group

Characteristics	Lean Group (B1)	Normal Group (B2)	Overweight Group (B3)	P-value
Total number of subjects	31 (15.66%)	148 (74.75%)	19 (9.59%)	0.174
Age, mean \pm SD	24.70 \pm 5.10	25.34 \pm 4.94	27.26 \pm 6.22	
Skin type				0.152
Dry	8 (25.81%)	39 (26.35%)	5 (26.32%)	
Neutral	14 (45.16%)	86 (58.11%)	10 (52.63%)	
Oil	5 (16.13%)	12 (8.11%)	1 (5.26%)	
Mixed	4 (12.9%)	11 (7.43%)	3 (15.79%)	
Sleep habit				0.442
Early bedtime	11 (35.48%)	57 (38.51%)	10 (52.63%)	
Late bedtime	20 (64.52%)	91 (61.49%)	9 (47.37%)	
Sleep duration per day (h)	7.42 \pm 0.5	7.61 \pm 0.89	7.26 \pm 0.8	0.154
Dietary habit				0.164
Meat-based	2 (6.45%)	22 (14.86%)	5 (26.32%)	
Vegetarian	6 (19.36%)	30 (20.27%)	3 (15.79%)	
Balance of vegetables and meat	23 (74.19%)	96 (64.87%)	11 (57.89%)	

Note: Late bedtime was classified as after 11:00 PM.

above three types of BMI were classified and divided into three groups, the lean group (B1), normal group (B2), and overweight group (B3). Basic information on the participants in each group is shown in [Table 1](#).

Skin Physiological Parameter Data Collection

All subjects were required to not use skin care products or cosmetics after washing their faces the night before the day of measurements and testing. The skin parameters were measured under controlled conditions (temperature, 20–22°C; relative humidity, 40%–60%), and the subjects were required to sit in these conditions for 30 minutes prior to the tests.

All measurements were taken with various probes attached to an MPA580 multi-probe adaptor system (Courage & Khazaka Electronic GmbH, Cologne, Germany). Skin hydration in the stratum corneum was measured using the Corneometer CM825, and sebum content was measured using the Sebumeter SM 815. TEWL was assessed using evaporimetry (Tewameter 300; Courage & Khazaka). Skin pH value was directly measured using the Skin-pH-Meter PH 905 (Courage & Khazaka). Skin melanin and haemoglobin contents were measured using the Mexameter MX18. Skin elasticity (R2) and firmness (F4) were measured using a Cutometer MPA580.

Collection of Skin Microbial Samples

Facial microbial samples were collected using a sterile swab dipped in a wetting solution (0.9% NaCl and 0.1% Tween-20) that was repeatedly scraped at least 30 times over a 3 cm \times 3 cm area of the left cheek, placed in a sampling tube, sealed, and stored in a –80°C refrigerator before extracting the DNA.

DNA Extraction and PCR

Microbial genomic DNA was extracted from skin swabs using the FastDNA Spin Kit (MP Biomedicals, USA) in accordance with the kit instructions. The hypervariable region V3–V4 of the bacterial 16S rRNA gene was amplified with primer pairs 338F (5'-ACTCCTACGGGAGGCAGCAG-3') and 806R (5'-GGACTACHVGGGTWTCTAAT-3') using an ABI GeneAmp 9700 PCR thermocycler (ABI, CA, USA). Meanwhile, the fungal endogenous transcribed spacer (ITS1–ITS2) was amplified by PCR with the forward primer ITS1F (5'-CTTGGTCA TTAGAGGAAGTAA-3') and the reverse primer ITS2R (5'-GCTGCGTTCTTCA TCGA TGC-3').

Gene Sequencing and Data Processing

Library construction was performed using the Nextflex Rapid DNA-Seq kit (Bio Science, USA). Sequencing was performed using MiseqPE300 (Illumina, USA). Raw data were uploaded to the NCBI Sequence Reads Archive database (accession number: SRP332768). Quality control of raw sequencing data was performed using FASTP software (v0.19.6), and splicing was performed using Flash software (v1.2.11). Sequences were classified using Uparse software (v7.0.1090) and annotated based on 97% similarity, and Silva 16S rRNA data were compared against the UNITE ITS database with the comparison threshold set to 0.7.

The raw data from high-throughput sequencing were collated and filtered, and valid sequences were obtained for subsequent analysis. Valid sequences of approximately 4,830,840 (16S rRNA) and 7,158,100 (ITS) were obtained. All samples were expanded by minimal sequence number, and 13,942 operational taxonomic units (OTUs) of bacterial copolymeric classes, belonging to 60 phyla, 6029 genera, and 4771 species, were identified. In addition, the copolymeric classification of 3949 fungal OTUs showed that the fungi belonged to 13 phyla, 677 genera, and 1225 species.

Statistical Analysis

IBM SPSS Statistics 26.0 software was used to analyse and process the data, and all data were expressed as mean \pm standard deviation (SD). Non-parametric test and Kruskal–Wallis test were selected to analyze the differences between groups in skin physiological parameters. While non-parametric Wilcoxon rank-sum test was used to compare microbial diversity and composition between the two groups. To compare the β -diversity between two groups, unweighted distance metrics were used. Spearman rank correlation test was used to determine the Spearman correlation between the biophysical parameters and the microbiota.

Results

Characteristics of the Subjects

The characteristics of the volunteers in the three BMI groups – the lean group (B1), the normal group (B2), and the overweight group (B3) – are shown in Table 1. As expected, the distribution of BMI in the volunteers followed a normal distribution. The proportion of female volunteers of normal weight was 70%, and the proportion of overweight and obese females was 10%, which is basically consistent with proportions reported in the China Population Health Data Report in 2021. We also summarised the skin types (dry, neutral, oily, and mixed) and sleep and dietary habits of the volunteers in each group. Neutral skin was seen in the highest number of participants, and there were no obvious differences in the proportions of skin types among the three groups. Additionally, there were no significant differences in the average age or sleep habits of the groups. However, we observed some differences in the dietary habits among the groups. The overweight group (B3) ate diets with a higher proportion of meat-based produce and a relatively poorer balance of meat and vegetables than the lean (B1) and normal (B2) groups.

Comparison of Physiological Skin Parameters in Each Group

The physiological parameters of the volunteers in the three groups are shown in Figure 1A–H. Moving from the lean group (B1) to the overweight group (B3), skin hydration in the stratum corneum tended to decrease, while sebum content tended to increase, but there were no significant differences ($p = 0.084, 0.14$; Figure 1A and D). Compared with the normal group (B2) and the lean group (B1), the overweight group's (B3) TEWL was significantly increased ($p = 0.009$; Figure 1B), indicating that the skin barrier was impaired. Moving from the lean group (B1) to the overweight group (B3), skin surface pH significantly decreased ($p = 0.007$; Figure 1C) and skin haemoglobin content ($p = 0.004$; Figure 1F) significantly increased. Skin firmness (F4) (Figure 1H) tended to increase with increasing BMI, but there was no significant difference among the three groups. Skin melanin content (Figure 1E) and elasticity value (R2) (Figure 1G) were also measured, but there were no obvious differences among the three groups. Compared with the lean (B1) and normal group (B2), the overweight group's physiological parameters were significantly different (B3). In contrast, there was no significant divergence in the physiological parameters of the cheek skin between the lean group (B1) and normal group (B2).

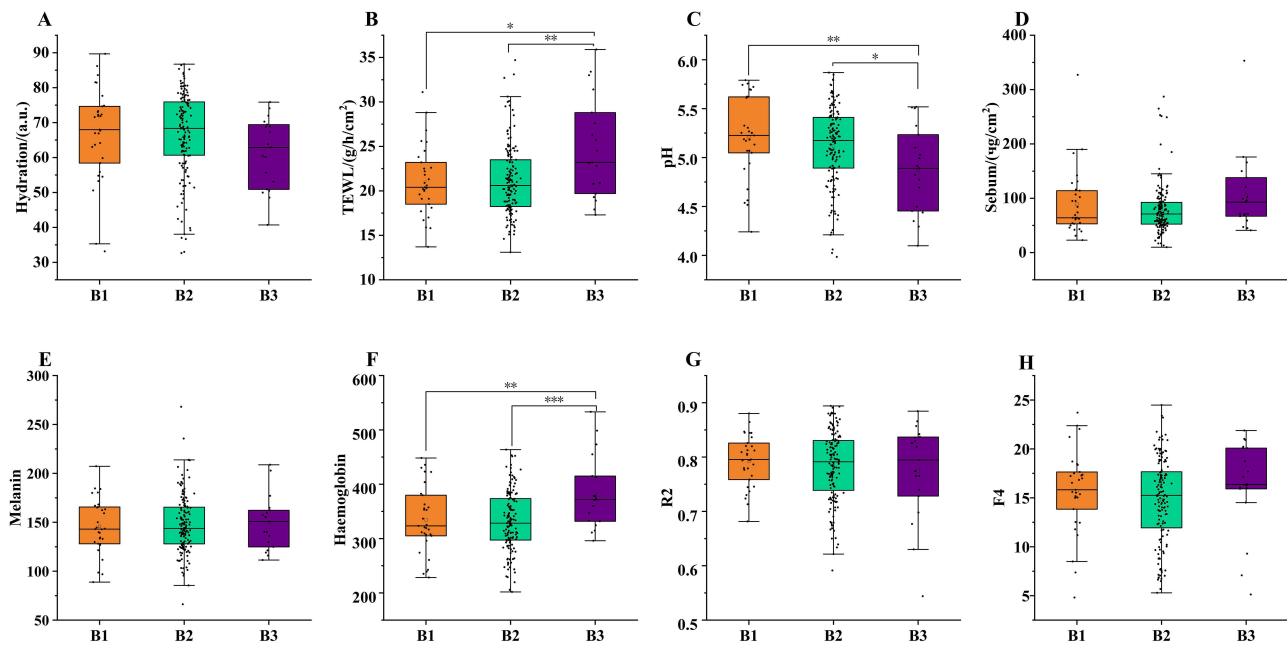


Figure 1 Comparison of physiological parameters in three groups. (A) Hydration; (B) TEWL; (C) pH; (D) Sebum; (E) Melanin; (F) Haemoglobin; (G) R2; (H) F4. Significant differences in the Figures are shown by * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

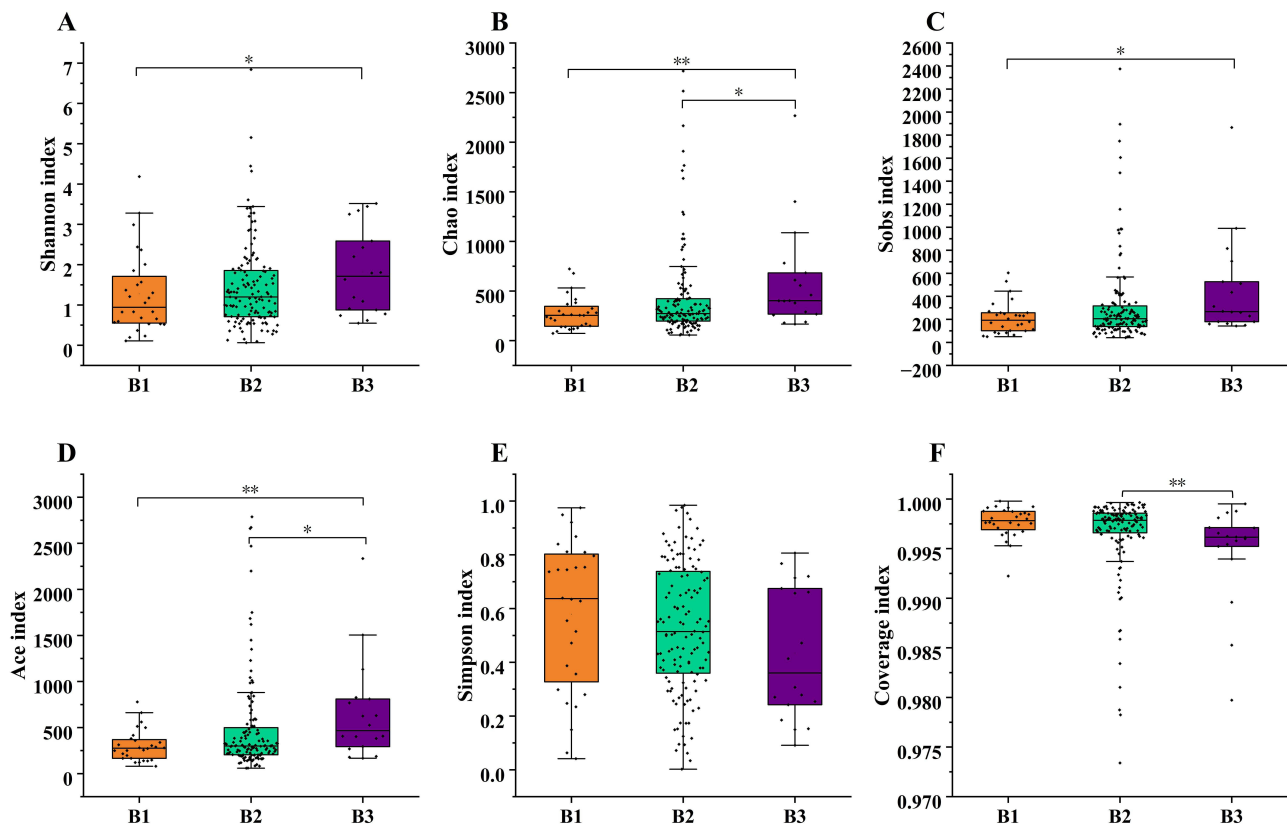


Figure 2 Bacterial diversity in three groups. (A) Shannon index; (B) Chao index; (C) Sobs index; (D) Ace index; (E) Simpson index; (F) Coverage index. Significant differences in the Figures are shown by * $p < 0.05$, and ** $p < 0.01$.

Alpha Diversity Analysis

The α -diversity in the three BMI groups was analysed using the Wilcoxon rank-sum test. Bacterial α -diversity in the three groups is shown in Figure 2A-F. Moving from the lean group (B1) to the overweight group (B3), the Shannon, Chao,

Sobs, and Ace indexes showed increases (Figure 2A-D). Moreover, compared with the lean group (B1), the overweight group's (B3) Shannon ($p = 0.032$; Figure 2A), Chao ($p = 0.003$; Figure 2B), Sobs ($p = 0.012$; Figure 2C), and Ace ($p = 0.004$; Figure 2D) indexes of bacterial diversity were significantly higher. Compared with the normal group (B2), the overweight group's Chao ($p = 0.026$; Figure 2B) and Ace ($p = 0.028$; Figure 2D) indexes were significantly higher and coverage ($p = 0.009$; Figure 2F) was significantly lower (B3).

The α -diversity of fungi among the three groups is shown in Figure 3A-F. Compared with the normal group (B2), the overweight group's (B3) Chao ($p = 0.096$), Sobs ($p = 0.1$), Ace ($p = 0.219$), and Simpson indexes were higher, and the coverage index was lower, although there were no significant differences ($p > 0.05$). These findings indicate that the species richness and diversity of the facial fungi microbiota were increased in the overweight group.

β -Diversity Analysis

Based on the unweighted_unifrac algorithm distance metrics, principal coordinate analysis was used to evaluate the β -diversity of the three BMI groups. There was no significant difference in β -diversity among the three groups ($p > 0.05$) (data not shown), indicating that the overall species composition and relative abundances of bacteria and fungi among the three groups were similar.

Differences in the Taxonomic Profiles of Skin Bacteria and Fungi Among the Three Groups

At the phylum level, the cheek bacteria of the three groups (Figure 4A) were mainly composed of *Actinobacteria*, *Firmicutes*, *Proteobacteria*, and *Bacteroidetes*. As the BMI increased, there was a decrease in *Actinobacteria* abundance and an increase in *Firmicutes* abundance. As can be seen in Figure 4B, the fungal genera of the cheeks mainly comprised *Ascomycota*, *Basidiomycota*, and unclassified-k-Fungi.

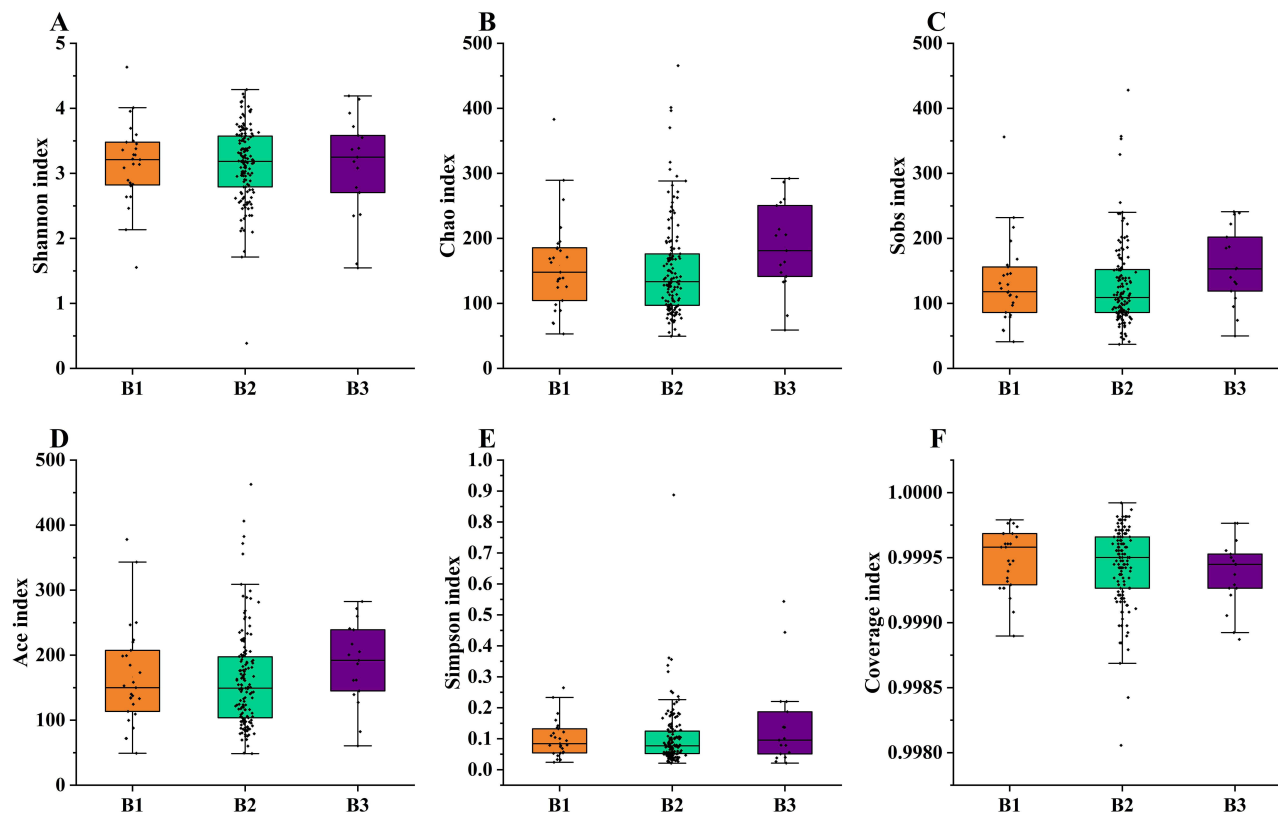


Figure 3 Fungal diversity in three groups. (A) Shannon index; (B) Chao index; (C) Sobs index; (D) Ace index; (E) Simpson index; (F) Coverage index.

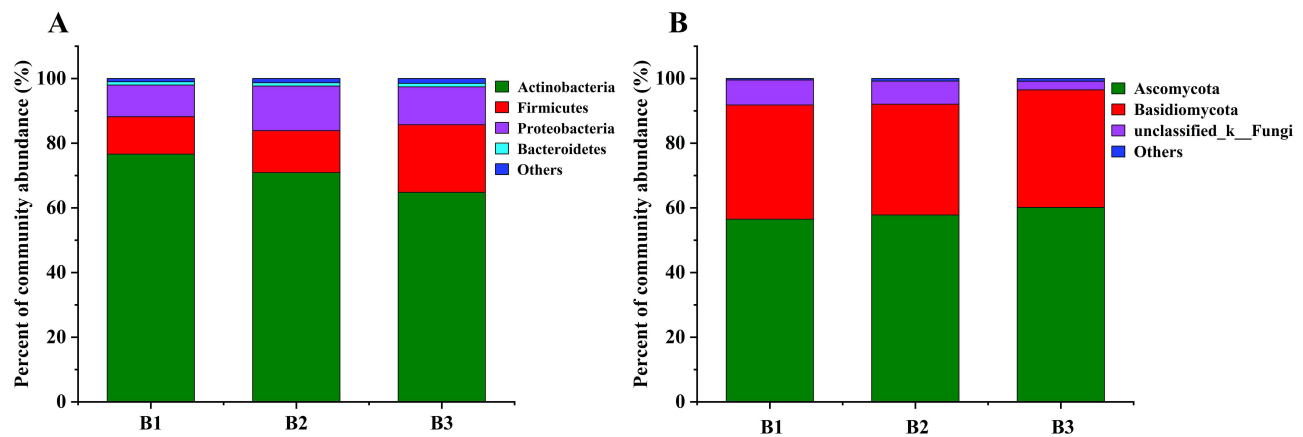


Figure 4 Differences in the relative abundances of skin bacteria and fungi at the phylum level in three groups. (A) Bacterial abundance; (B) Fungal abundance.

At the genus level, cheek bacteria were mainly composed of *Cutibacterium*, *Staphylococcus*, *Pseudomonas*, *Neisseriaceae*, *Rhodococcus*, *Corynebacterium*, *Streptococcus*, *Stenotrophomonas*, and *Ralstonia* (Figure 5A). As the BMI increased, we observed a decrease in *Cutibacterium* abundance and an increase in *Staphylococcus* abundance, resulting in an increase in the *Staphylococcus* to *Cutibacterium* ratio. As BMI increased, the abundance of *Corynebacterium* tended to increase (Figure 5C). The abundances of *Corynebacterium* ($p = 0.024$) and *Streptococcus* (Figure 5B, $p = 0.031$) were significantly higher and that of *Neisseriaceae* ($p = 0.043$) was significantly lower in the overweight group (B3) than in the normal group (B2). Linear discriminant analysis effect size (LEfSe) was conducted to demonstrate the differences in OTUs between the overweight group (B3) and normal group (B2) (Figure 5G). A taxonomic cladogram identified the taxa with the greatest differences in abundance between the overweight group (B3) and normal group (B2). Compared with the normal group (B2), the overweight group (B3) had more bacteria belonging to the *Corynebacterium* and *Streptococcus* genera.

The cheek fungi were mainly composed of *Aspergillus*, *Cladosporium*, *Cutaneotrichosporon*, unclassified_K_Fungi, *Malassezia*, *Rhodotorula*, *Wallemia*, *Alternaria*, *Penicillium*, *Candida*, *Fusarium*, and *Nigrospora* (Figure 5B). As the BMI increased, the abundances of *Aspergillus*, unclassified_K_Fungi, and *Rhodotorula* genera tended to decrease, while those of *Cladosporium* and unclassified_o_Hypocreales genera tended to increase. The abundances of *Malassezia* (Figure 5E, $p = 0.003$) and *Candida* (Figure 5F, $p = 0.016$) were significantly higher and that of *Cutaneotrichosporon* ($p = 0.049$) was significantly lower in the overweight group (B3) than the normal group (B2). Similarly, compared with the normal group (B2), the lean group's (B1) abundance of *Malassezia* and *Candida* also showed an upward trend. LEfSe was conducted to demonstrate the differences in OTUs between the overweight group (B3) and normal group (B2) (Figure 5H). A taxonomic cladogram identified the taxa with the greatest differences in abundance between the overweight group (B3) and normal group (B2). Compared with the normal group (B2), the overweight group (B3) had more bacteria belonging to the *Malassezia* and *Candida* genera.

Correlation Analysis of the Skin Microbiota and Physiological Parameters

Spearman correlations among skin physiological parameters (hydration, TEWL, sebum, pH, melanin, haemoglobin, R2, and F4) and skin bacteria and fungi were analysed and summarised in a correlation heatmap (Figure 6). The relative abundance of *Malassezia* was significantly positively correlated with sebum content ($r = 0.169$, $p < 0.05$) and significantly negatively correlated with skin surface pH ($r = -0.207$, $p < 0.01$). Additionally, skin surface pH was significantly negatively correlated with the relative abundances of *Candida* ($r = -0.219$, $p < 0.01$) and *Cladosporium* ($r = -0.172$, $p < 0.05$) and significantly positively correlated with the relative abundance of unclassified_o_Ascomycota ($r = 0.17$, $p < 0.05$). This finding is consistent with the trend analysis of the previous physiological parameters and microbiota, showing that skin surface pH decreased and the relative abundances of *Malassezia*, *Candida*, and *Cladosporium* genera increased significantly from normal to overweight. Similarly, TEWL was positively associated with the abundances of *Staphylococcus* ($r = 0.124$, $p > 0.05$), *Cutibacterium*

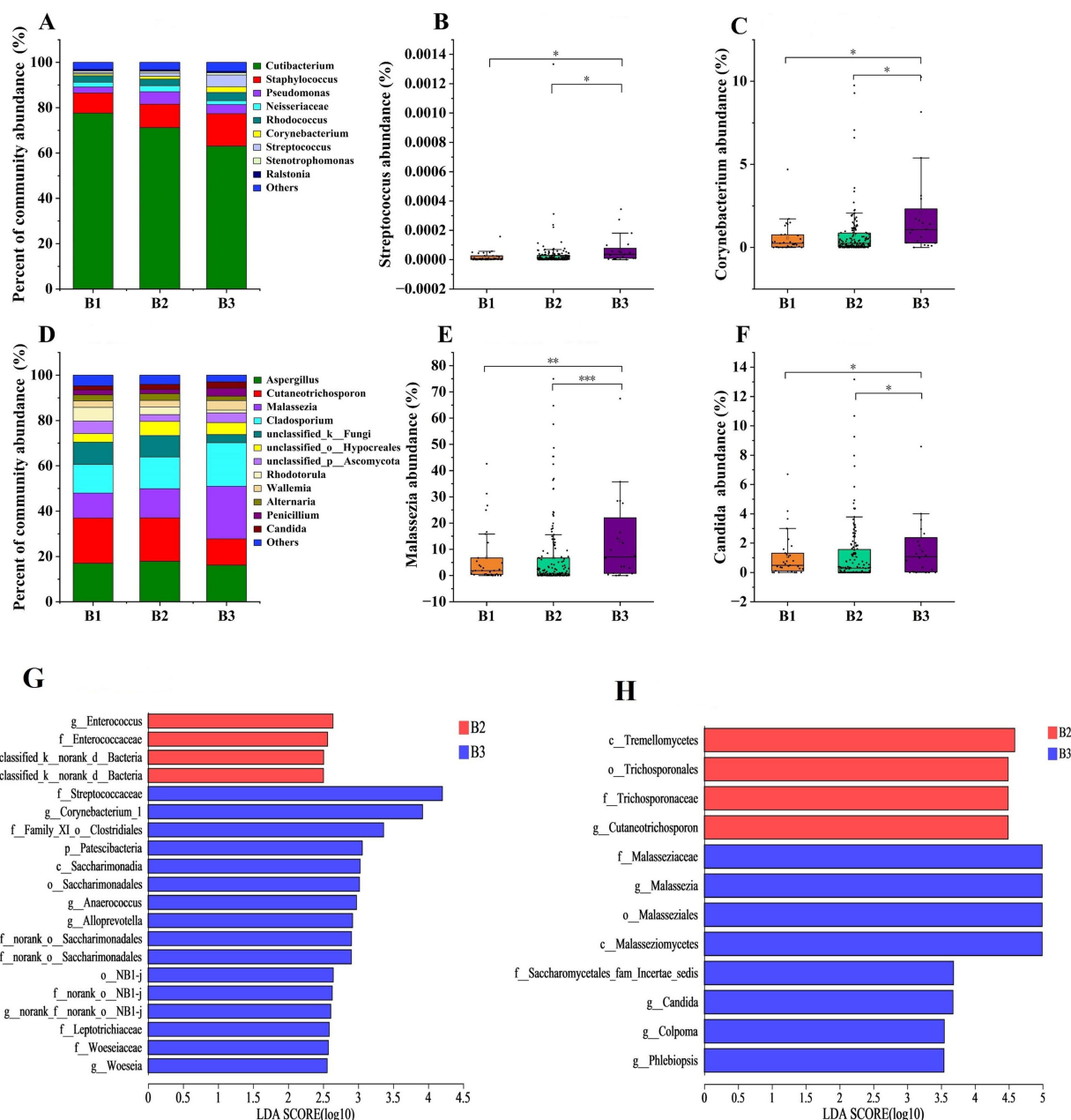


Figure 5 Differences in the relative abundance of the skin microbiota at the genus level in three groups. (A) Bacterial abundance; (B) *Streptococcus*; (C) *Corynebacterium*; (D) Fungal abundance; (E) *Malassezia*; (F) *Candida*. Significant differences in the Figures are shown by * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$. Differentially abundant genera and species between the B2 and B3 skin microbiomes, as identified using linear discriminant analysis effect size. (G) Bacteria with statistical significance cut-offs set at LDA > 2.5 and $p < 0.05$. (H) Fungi with statistical significance cut-offs set at LDA > 3.5 and $p < 0.05$.

($r = 0.141$, $p > 0.05$), *Cutaneotrichosporon* ($r = 0.218$, $p < 0.01$), unclassified_K_Fungi ($r = 0.174$, $p < 0.05$) and significantly negatively correlated with the abundances of *Neisseria* ($r = -0.267$, $p < 0.001$), unclassified_o_Hypocreales ($r = -0.165$, $p < 0.05$), and *Pseudomonas* ($r = -0.154$, $p < 0.05$). In addition, haemoglobin was positively correlated with the abundances of *Cutibacterium* ($r = 0.277$, $p < 0.001$), *Cutaneotrichosporon* ($r = 0.129$, $p > 0.05$), *Malassezia* ($r = 0.099$, $p > 0.05$), and unclassified_k_Fungi ($r = 0.225$, $p < 0.01$), but significantly negatively correlated with the abundances of *Pseudomonas* ($r = -0.252$, $p < 0.001$), *Stenotrophomonas* ($r = -0.229$, $p < 0.01$), and *Ralstonia* ($r = -0.228$, $p < 0.01$). Overall, there was a close correlation between the abundance of the skin microflora and skin physiological parameters. From the Spearman correlation heatmap, we observed an interesting significant correlations between some bacterial and fungal genera and age. Age was significantly

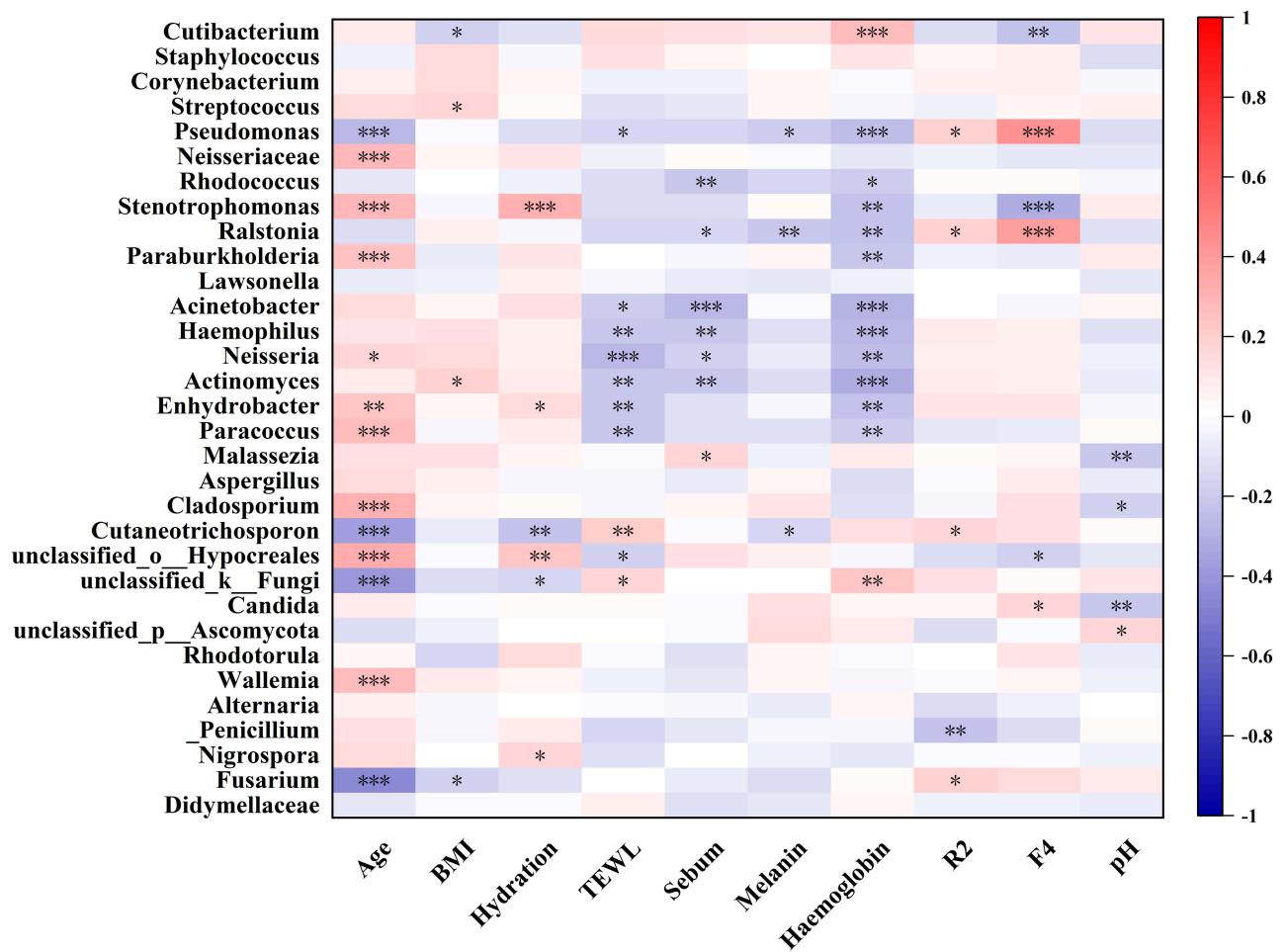


Figure 6 Spearman correlation analysis of facial bacterial, fungal abundance, and skin physiological parameters. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

positively correlated with the abundances of *Neisseriaceae* ($r = 0.287$, $p < 0.001$), *Stenotrophomonas* ($r = 0.299$, $p < 0.001$), and *Cladosporium* ($r = 0.309$, $p < 0.001$) and significantly negatively correlated with the abundances of *Pseudomonas* ($r = -0.278$, $p < 0.001$) and *Cutaneotrichosporon* ($r = -0.376$, $p < 0.001$).

Correlations between bacteria and fungi were also analysed using Spearman correlation analysis and summarised in a correlation heatmap (Figure 7). We observed that the abundance of *Staphylococcus* was significantly positively associated with the abundances of *Malassezia* ($r = 0.269$, $p < 0.01$), *Rhodotorula* ($r = 0.177$, $p < 0.05$), and *Wallemia* ($r = 0.196$, $p < 0.05$). The abundance of *Streptococcus* was significantly positively associated with the abundances of *Cladosporium* ($r = 0.179$, $p < 0.05$) and *Candida* ($r = 0.156$, $p > 0.05$) and significantly negatively correlated with the abundance of *Didymellaceae* ($r = -0.171$, $p < 0.05$). The abundance of *Corynebacterium* was positively associated with that of *Malassezia* ($r = 0.137$, $p > 0.05$). Additionally, the abundance of *Pseudomonas* showed a significant positive correlation with the abundances of *Aspergillus* ($r = 0.193$, $p < 0.05$) and *Candida* ($r = 0.196$, $p < 0.05$). The abundance of *Neisseriaceae* was significantly negatively correlated with the abundances of *Cutaneotrichosporon* ($r = -0.271$, $p < 0.01$) and *Fusarium* ($r = -0.245$, $p < 0.01$) and positively correlated with the abundance of *Nigrospora* ($r = 0.178$, $p < 0.05$).

Discussion

The prevalence of overweight and obesity has increased worldwide in recent years and has developed into a significant public health problem. It has been demonstrated that obesity is a major risk factor for metabolic and dermatological diseases.^{3,6,9,26} An abundance of work has focused on the skin physiology and manifestations of obesity-associated skin diseases, but little is known about the correlations between BMI, facial physiological parameters, and the skin

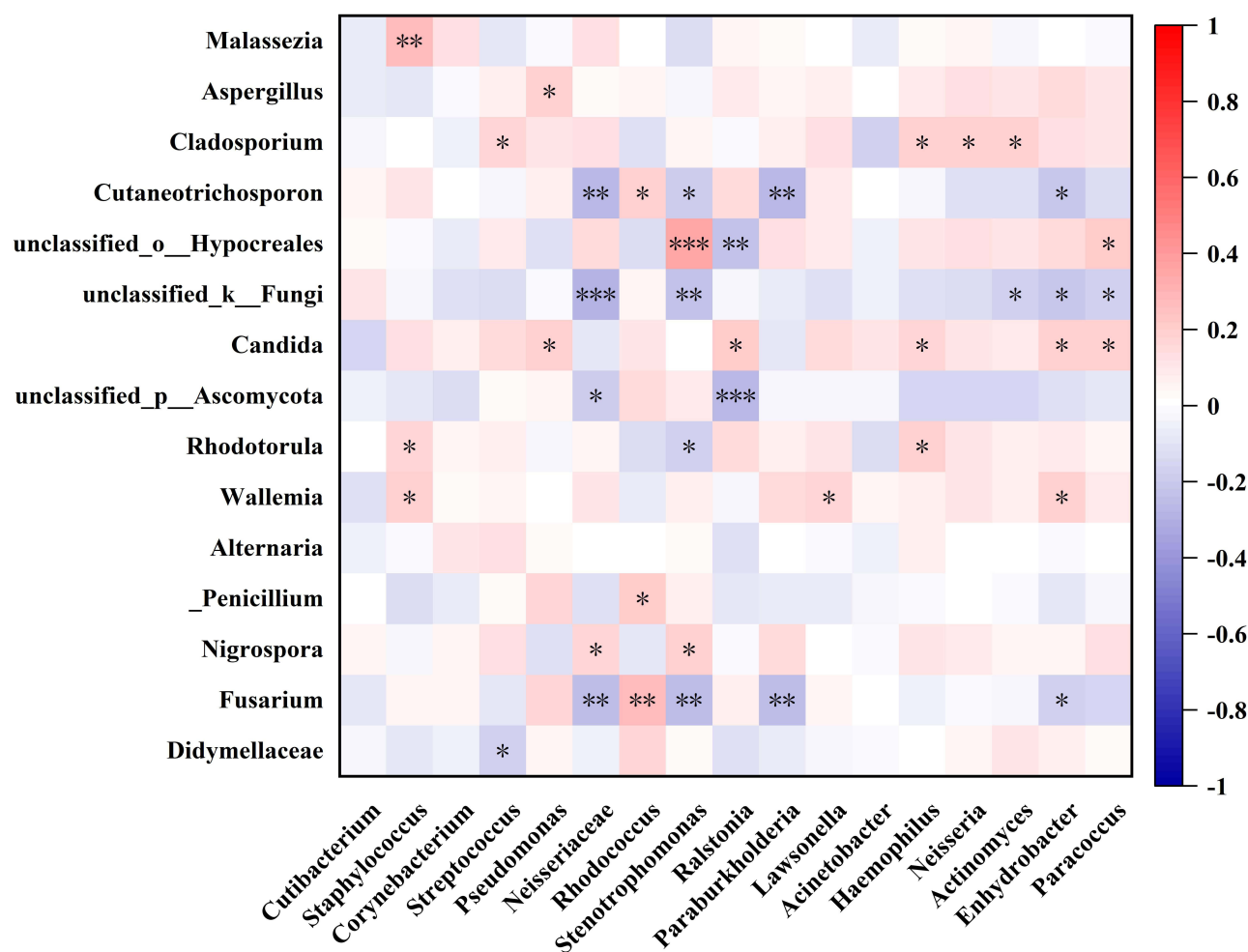


Figure 7 Spearman correlations between facial bacterial and fungal abundance. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

microbiome for healthy individual. Thus, to the best of our knowledge, the current study is the first to attempt to investigate the correlations between BMI and facial skin physiological parameters, as well as the facial skin microbiome. A total of 198 Chinese women of different BMI grades, aged 18–35, and living in Shanghai were investigated. Surprisingly, in our research, we found that BMI was associated with physiological changes in the facial skin and facial bacterial and fungal flora, and there were close correlations among these factors.

Our study found facial skin physiological parameters typically differed between the lean group (B1) and the overweight group (B3), with the latter showing increased TEWL, sebum content, and haemoglobin content and decreased skin pH and skin hydration in terms of the stratum corneum water content, although differences in some of the parameters were nonsignificant (Figure 2). The increased TEWL indicated that skin barrier function in the overweight group (B3) was impaired. Many studies have provided evidence that skin diseases or even systemic diseases can result when the skin barrier is broken or when the balance between commensals and pathogens is disturbed.^{27,28}

Various changes in barrier integrity, such as xerosis and altered TEWL, have been linked to obesity. Xerosis is a common feature related to skin hydration changes in morbidly obese patients.^{29,30} In a cross-sectional study of 1300 patients, obesity was found to significantly affect the stratum corneum moisture content.³¹ Additional studies revealed that individuals with rosacea had higher TEWL rates and lower skin hydration than the normal controls.³² In addition, Nino et al found significantly higher TEWL values on the forearms ($p < 0.05$) of children with obesity than on those of children of a normal weight.³³ In a study of the correlations between BMI and epidermal biophysical properties, BMI was also negatively correlated with stratum corneum hydration of both the forearm and the shin in women.³⁴ Our results

further confirm these previous findings,³⁵ as we found correlations between TEWL, skin hydration, and BMI. However, our results are inconsistent with the findings of some studies that found that BMI was not associated with stratum corneum hydration, including in middle-aged and older adult populations.^{36,37}

Many studies have focused on ascertaining the correlations between skin surface pH and incidence of skin diseases.^{38–40} BMI has been confirmed to be positively correlated with skin surface pH. Skin surface pH was higher in the inguinal folds of diabetic women with a BMI > 25 kg/m², and a high pH increases the risk of developing skin infections.³⁴ A comparative study of the vulvar and abdominal skin microbiota of healthy females showed that the vulvar pH of women with a high BMI was significantly higher than that of women with average BMIs.²¹ In our results, the cheek pH of the overweight group (B3) was significantly lower than that of the lean (B1) and normal (B2) groups, which is inconsistent with the skin surface pH findings for the forearm, shin, inguinal folds, vulva, and abdomen of females with a high BMI.^{21,34} This discrepancy might be caused by different physiological characteristics of the different skin sites. Facial skin is typically a site of highly acidic oily skin and is characterised by the presence of bacteria (eg, *Corynebacterium minutissimum* and *Cutibacterium* spp.) that consume lipids.^{11,41} In the current study, we observed that healthy females with a high BMI had increased skin sebum (Figure 1D), which is easily hydrolysed to fatty acids, reducing the skin surface pH.³⁸ Moreover, we also saw a higher abundance of *Streptococcus* ($p = 0.031$), *Corynebacterium* ($p = 0.024$), *Malassezia* ($p = 0.003$), and *Candida* ($p = 0.016$) in the overweight (high-BMI) group (B3), and the metabolites of these species can also affect skin surface pH.

Haemoglobin levels reflect vascular activity, and an increase in skin haemoglobin content often manifests as skin inflammation, which affects the appearance of the skin.⁴² Obesity is known to be a major risk factor for inflammatory skin diseases, including atopic dermatitis and psoriasis. The inflammatory cytokines produced by adipose tissue and the activation of innate immunity are considered important factors in obesity-induced inflammation.²⁶ In our study, skin haemoglobin content increased significantly with an increase in BMI, which is consistent with the findings of previous studies. Loffler et al demonstrated that a higher BMI was significantly associated with an increase in skin blood flow.³⁵ These alterations in skin microcirculation may be the result of physiological compensation. Jongh et al first reported that obesity was associated with impaired cutaneous microvascular function compared with a lean composition.⁴³ Correlation analysis showed that haemoglobin content was positively correlated with the abundances of *Cutibacterium* ($p < 0.001$), *Malassezia* ($p > 0.05$), and unclassified_k_Fungi ($P < 0.01$) and negatively correlated with those of *Pseudomonas* ($p < 0.001$), *Neisseriaceae* ($p > 0.05$), *Rhodococcus* ($p < 0.05$), *Corynebacterium* ($p > 0.05$), *Streptococcus* ($p > 0.05$), and other strains that prefer humid environments. Changes in the skin's physiological conditions affect the microbiota. Similarly, the abundances of these bacterial genera differed, which would cause differences in metabolites and pro-inflammatory factors, changes that may also have affected skin haemoglobin levels. These findings suggest that the epidermal barrier is fundamentally altered in the obese population, and these phenomena are worth researching further.

Our findings revealed that the Shannon, Sobs, Ace, and Chao indexes were increased in the high-BMI population (B3 group), suggesting that a high BMI induces both the abundance and diversity of facial bacterial and fungal microbiota (Figures 2 and 3). Brandwein et al compared the skin bacterial microbiota diversity indices of different BMI populations and found that the Shannon index was significantly lower in the high-BMI population than in the normal BMI population.²⁰ Although Brandwein et al did not describe from where exactly on the body the skin samples were collected, based on the composition of the skin microbiota (mainly *Staphylococcaceae* and *Corynebacteriaceae*), we speculated that it was not the facial skin. As has been shown, there are differences in the composition and abundance of the microbiota in different skin sites. The Shannon index of the vulvar skin microbiota was higher in healthy females with a high BMI than in females with an average BMI, indicating that a high BMI is associated with a high α -diversity.²¹ Here, we first reported that the diversity of the microbiota, including bacteria and fungi, was higher in the facial skin of individuals with a high BMI.

In a comparison of the vulvar and abdominal skin microbiota of healthy females with a high and average BMI, the abdominal skin microbiota was not affected by BMI status, while bacterial community modulations in the vulva were associated with BMI.²¹ Our results revealed that BMI causes changes in the bacterial abundance of facial skin (Figure 3). Compared with the normal group (B2), the overweight group (B3) had higher abundances of *Streptococcus*, *Corynebacterium*, *Malassezia*, and *Candida* and lower abundances of *Neisseriaceae* and *Cutaneotrichosporon*.

Concurrently, we observed differences in the abundances of predominant skin species among the BMI groups. *Cutibacterium acne* and *Staphylococcus epidermidis*, which are predominant species of the facial skin, are also known as sentinel bacteria and play a crucial role in maintaining skin homeostasis.¹² In our study, it was interesting to observe that the abundance of *Cutibacterium* decreased, while that of *Staphylococcus* increased as BMI increased (Figure 5), and this led to an elevation in the *Staphylococcus* to *Cutibacterium* ratio. Obesity alters the composition of skin lipids, leading to skin colonisation by lipophilic bacteria and intestinal colonisation by pro-inflammatory species. These changes impair epithelial barriers and promote Th17 responses, which may increase the risk of inflammatory skin diseases, including eczema, atopic dermatitis, and psoriasis.⁴⁴ Studies have shown that methicillin-resistant *Staphylococcus aureus* infections are more common in obese patients.^{45,46} The severity of atopic dermatitis symptoms correlated well with BMI, and the abundance of *S. aureus* in the skin of patients with eczema was significantly higher than in that of people with healthy skin.⁴⁷ In addition, a significantly increased risk of rosacea was described for patients with high BMI.⁴⁸ A retrospective cohort study found that obesity patients were more likely to have diabetic foot ulcers and methicillin-resistant *S. aureus* infections.⁴⁹ Similarly, the relative abundance of *Streptococcus* increased with BMI and was significantly different in the high-BMI group (B3) (Figure 5B). It has been shown that *Streptococcus* is normally present in the healthy skin microbiota and helps to maintain skin health, but changes in its abundance may lead to skin diseases.⁵⁰ Reportedly, the skin microbiome was more enriched with *Streptococcus* and less enriched with *Cutibacterium* in the lesion areas of patients with psoriasis than in their normal-appearing skin.⁵¹ An increased abundance of *Streptococcus* may pose risk to skin health.

In our results, the relative abundance of *Corynebacterium* was also significantly and positively correlated with BMI (Figure 5C), which is consistent with previous findings. Moestrup et al compared the skin microbiota of mice fed a high-fat diet with that of mice on a calorie-neutral (normal) diet and found that species of the *Corynebacterium* genus were the dominant bacteria in the high-fat diet group but were barely detectable in the normal diet group.⁵² Brandwein et al also found that *Corynebacterium* was significantly associated with BMI.²⁰ Another study demonstrated that *Corynebacterium* promoted skin inflammation in obese patients in an interleukin-23-dependent manner by expressing fungal acids, an activity that is highly conserved in *Corynebacterium* species, providing supporting evidence for an alternative relationship between *Corynebacterium* and obesity.⁵³ A study on healthy women of childbearing age found that the vulvar microbial community of women with a normal BMI was dominated by *Lactobacillus*, while that of women with a high BMI were mainly colonised by *Finegoldia* and *Corynebacterium*.²¹ In contrast, no changes in the association of the microbiota with BMI were observed in the exposed skin around the abdomen, suggesting that BMI affects the skin microbiota in a site-specific manner.

After summarising the previous research results, we can speculate that the skin of individuals with a higher BMI is more prone to colonisation by *Corynebacterium* strains. *Corynebacterium* species are part of the normal human and animal skin microbiome and are often abundant at moist sites. The increase in the abundance or excessive proliferation of *Corynebacterium* could lead to skin microbiota and skin homeostasis disorders and therefore skin problems.⁵³ For example, the excessive proliferation of *Corynebacterium* was found to cause excess body odour and even skin diseases in obese patients.⁵⁴ The abundance of *Corynebacterium* spp. significantly increased in the high-BMI group, which could increase the risk of skin infections such as erythrasma, trichomycosis, and pitted keratolysis.⁵⁵ Therefore, we believe that an elevation in BMI leads to changes in facial flora that may adversely affect skin health.

Studies into the associations between BMI and the skin microbiota have mainly focused on bacteria, and there has been relatively little research on fungi. Recent studies have shown that fungi play an important role in maintaining the balance of the skin microbiota. Researchers have also begun to elucidate the topographical diversity of fungal communities on human skin.⁵⁶ Compared with normal or lean individuals, obese patients tend to sweat more, and the increased subcutaneous fat increases the friction and moisture content of the skin, so they are more susceptible to skin diseases, such as secondary bacterial infections, *Candida* infection, and dermatophyte overgrowth.^{3,4,9} There is also evidence that gradual weight loss can significantly improve the severity of psoriasis.^{57–59} In the statistical analysis of facial skin fungal genera, we found that the abundances of *Malassezia* and *Candida* increased significantly with increasing BMI (Figure 5E and F). As is known, *Malassezia* is the dominant fungal genus of the skin, and a large number of studies have shown *Malassezia* to be associated with many skin diseases, including lichen planus, seborrheic dermatitis, and psoriasis.^{60–62}

Our findings provide further evidence that obese patients are more susceptible to fungal-related skin diseases than normal individuals, and that BMI is strongly associated with health. The abundance of *Candida* species significantly increased in the high-BMI group, which poses an increased risk of *Candida albicans* infections. There have been reports that *C. albicans* infections are more prevalent in obese patients than in normal or lean individuals, where they might cause folliculitis, intertrigo, furunculosis, or paronychia of the hands or feet.⁶³ Therefore, we could speculate that elevated BMI leads to changes in fungal flora that adversely affect skin health.

In our study, we were surprised to observe a close correlation between the abundances of bacterial and fungal microflora and skin physiological parameters, especially skin hydration, skin pH, sebum, and TEWL. It has been confirmed that obesity affects sebaceous secretion and sweat gland secretion, as well as skin surface temperatures.⁵² These changes impact the lipid composition of the skin, changing the environment in which microorganisms inhabit and the available nutrition, leading to alterations in microbial abundance and structure.⁶⁴ Skin pH displayed a significantly negative correlation with the abundances of *Malassezia*, *Candida*, and *Cladosporium* and a significantly positive correlation with the abundance of unclassified_p_Ascomycota (Figure 6). We are inclined to conclude that when the skin microenvironment changes, manifested as variations in skin hydration, sebum, and pH value, the abundances of these bacteria alter accordingly. However, it is still unclear if these events are linked, and what the direction of causality is between them. This needs to be further substantiated via additional studies.

A large number of studies have confirmed that obesity alters the diversity and abundance of the gut microbiota, affects lipid metabolism, alters the composition and structure of skin lipids, damages the barrier function of the skin, changes the diversity and abundance of the skin microbiota, and disturbs skin microbiota homeostasis, all of which in turn lead to skin disorders and diseases.^{30,52,65,66} As we known, changes in the dietary structure, especially an increased intake of high-fat foods, are the main causes of obesity. Additionally, research has demonstrated that supplementing diets with probiotics, prebiotics, and omega-3 fatty acids increases skin moisture content, reduces TEWL values, and enhances skin barrier function.⁶⁷ By using specific dietary interventions to improve the condition of the skin, encouraging results have been achieved in the clinical adjuvant treatment of acne, atopic dermatitis, and other skin conditions.⁶⁸ An effective approach for overweight and obese individuals to improve their body and skin condition is to reduce their BMI through specific dietary interventions.

Conclusions

In conclusion, the results in this study demonstrated that BMI was associated with differences in the biophysical properties and microbiome of the facial skin in healthy individuals. In addition, a high BMI affects the integrity of skin barrier and changes the skin flora diversity and species composition, which increases the risk of skin disorders and even diseases. Spearman correlation analysis revealed strong correlations between the microbiota and the physiological parameters. Therefore, BMI is an important factor affecting skin health, and achieving a reasonable body weight is essential to maintaining skin health for overweight and obese people.

Data Sharing Statement

The sequence dataset has been deposited in the NCBI Sequence Reads Archive Database (Accession Number: SRP330206).

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Disclosure

The authors declare no competing interests in this work.

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