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ORIGINAL RESEARCH

Analysis of the Facial Skin Bacterial Community in Vietnamese Individuals with Sensitive Skin and Clinical Relevance

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ABSTRACT

***Introduction*:** Sensitive skin (SS) is a common clinical condition characterized by exaggerated sensory responses such as burning, stinging, itching, and irritation to otherwise non-pathological stimuli, most frequently affecting the face. The underlying mechanisms remain incompletely understood, particularly with regard to the role of the skin microbiome.

***Methods*:** This study investigated the facial skin microbiota in Vietnamese adults with SS and examined its associations with clinical symptoms and skin physiological parameters. A total of 75 participants were enrolled, including 45 with SS and 30 with nonsensitive skin (NSS). Clinical assessment included evaluation of subjective symptoms, symptom regularity, time of symptom onset, trigger factors, and objective measurements of skin pH, sebum, hydration, transepidermal water loss (TEWL), erythema, and melanin index. Bacterial communities were profiled using 16S rRNA gene sequencing targeting the V3–V4 region.

***Results*:** Participants with SS exhibited significantly higher erythema and TEWL across all sex and age subgroups, as well as elevated skin pH in female and middle-aged participants ($p < 0.05$). Alpha and beta diversity metrics did not differ significantly between SS and NSS groups. However, differential abundance analysis using Analysis of Compositions of Microbiomes with Bias Correction (ANCOM-BC) identified 53 bacterial genera with significant compositional differences, indicating subtle community restructuring. A total of 32 genera, including *Peredibacter*, *Enterobacter*, and *Marmoricola*, were enriched in SS, whereas *Streptococcus*, *Escherichia-Shigella*, and *Weissella* were depleted. Correlation and stratified analyses further revealed genus-level associations with skin physiological parameters, clinical symptoms, anatomical locations,

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symptom regularity, and time since symptom onset.
Conclusions: SS is associated with subtle but distinct alterations in facial skin microbiome composition, in parallel with measurable changes in skin physiological parameters related to barrier function and reactivity. The results indicate associations between microbial composition, skin physiological parameters, and clinical characteristics in the SS phenotype, and offer a population-specific microbiome reference for Vietnamese facial skin.

Keywords: Sensitive skin; Facial microbiota; 16S rRNA sequencing; Transepidermal water loss; Erythema; Skin physiology

Key Summary Points

Why carry out this study?
Sensitive skin (SS) is commonly reported in adults and predominantly affects the face, where subjective sensory complaints are frequent but routine assessment remains challenging due to the lack of well-tolerated and standardized objective markers; meanwhile, potential biological contributors, including the skin microbiome, remain insufficiently characterized.
Evidence integrating microbiome composition with clinical symptom patterns and objective biophysical parameters in SS remains limited, particularly in underrepresented populations such as Vietnamese adults.
This study asked whether Vietnamese adults with SS show distinct facial skin bacterial community features compared with nonsensitive skin (NSS), and whether these microbial patterns are associated with clinical characteristics and skin physiological parameters.
What was learned from the study?
This study contributes to understanding how facial skin bacterial composition relates to sensitive skin in Vietnamese adults when considered alongside clinical symptoms and skin biophysical parameters.
Sensitive skin showed higher transepidermal water loss and erythema, with subgroup-specific pH differences, while overall bacterial alpha and beta diversity did not differ significantly; however, genus-level differential abundance analysis identified distinct compositional differences associated with clinical symptom characteristics and skin physiological parameters.
The study provides a population-specific reference of the facial skin microbiome in Vietnamese adults, which may be useful for future studies on sensitive skin.

INTRODUCTION

Sensitive skin (SS) was initially described as cosmetic intolerance syndrome [1] and later termed *status cosmeticus* [2]. Beyond cosmetic intolerance, subsequent studies revealed that environmental factors such as cold, heat, ultraviolet light (UV) exposure, pollution, and humidity can similarly provoke unpleasant sensation of stinging, burning, or tightness without visible lesions [3]. Consequently, the term has evolved into sensitive skin syndrome [4, 5], encompassing synonymous concepts such as reactive, irritable, or intolerant skin [6, 7]. Epidemiological surveys indicate that approximately 71% of adults report some degree of skin sensitivity, and about 40% describing moderate-to-severe manifestations [8]. These symptoms are most frequently localized to the face, likely due to its greater environmental exposure, thinner stratum corneum, and higher density of sensory nerve endings [8].

The lactic acid stinging test (LAST), employing 5–10% lactic acid solution, has long been considered the classical method for assessing cutaneous sensitivity [7, 9, 10]. However, despite its objectivity, LAST often induces discomfort and lack standardization of reagents, limiting its clinical application. To overcome these limitations, patient-reported outcome scales, such as the Sensitive Scale-10 (SS-10), have therefore been introduced to quantify symptom severity and treatment response while avoiding procedural discomfort [11]. These subjective assessments correlate strongly with instrumental parameters and display consistent prevalence across Fitzpatrick skin types [12], supporting their use as reliable indicators of sensitivity.

Biophysical investigations have revealed that SS overlaps with barrier-impaired dermatoses such as atopic dermatitis and acne, where erythema, papules, or vesicles may occasionally appear [4, 13]. Mechanistically, increased transepidermal water loss (TEWL) and reduced stratum corneum capacitance are frequently observed, reflecting impaired barrier integrity [10, 14]. Accordingly, quantitative evaluation of pH, TEWL, stratum corneum hydration (SCH), sebum level, and erythema index provides objective insight into barrier homeostasis [4, 15–17].

Nonetheless, as the body's primary defense against pathogens, the skin is essential for maintaining a stable barrier system, comprising physical, chemical, and microbial components [18, 19]. The diversity of bacterial species inhabiting the skin surface and its outermost layers has been shown to correlate with various dermatologic conditions, often through differences in their relative abundances [20–25]. Each individual harbors a distinct microbial community that can either support cutaneous health or increase susceptibility to irritation and inflammation [26]. This community includes both beneficial and potentially harmful microorganisms, as well as transient and resident taxa [27, 28], all of which modulate the skin barrier and the innate immune responses of the epidermis [29, 30]. The skin microbiome plays a pivotal role in preventing pathogen colonization, shaping immune maturation, and metabolizing host-derived compounds, functions comparable to those of the gut microbiome [31]. However, because the skin is a relatively open and externally exposed environment, interindividual variation in microbial composition is substantial, rendering the cutaneous microbiome less complex and more dynamic than that of the gut. Despite increasing interest, the precise relationship between the skin's bacterial community and sensitive skin remains insufficiently characterized, particularly regarding its clinical relevance across both subjective and objective dimensions.

Therefore, the present study aimed to characterize the facial skin bacterial community in Vietnamese individuals with SS compared with those with NSS, using 16S rRNA (V3-V4) gene sequencing combined with comprehensive clinical characterization and biophysical measurements. By correlating microbial diversity and taxonomic composition with detailed clinical features, including symptom type, onset, regularity, facial distribution, and trigger factors, as well as objective parameters such as TEWL, pH, hydration, sebum, melanin, and erythema, this study seeks to better delineate microbial patterns associated with SS and contributing factors of SS. The findings are expected to improve understanding of the clinical and microbiome characteristics of sensitive skin and to provide a population-specific microbiome reference for Vietnamese facial skin.

METHODS

Subjects

Patients aged 18–55 years who attended the Department of Dermatology and Skin Aesthetics, University Medical Center, Ho Chi Minh City, Viet Nam from November 2024 to April 2025 for a skin examination were recruited. Participants were classified as having SS if they were clinically diagnosed by a board-certified dermatologist, presented at least one characteristic symptom (itching, stinging, irritation, burning, pain, erythema, and uneven skin texture), and met diagnostic criteria defined by a 10% lactic acid

sting test (LAST ≥ 3) and SS-10 score ≥ 13 [32]. Symptom regularity (intermittent or persistent), time of symptom onset, and potential triggering factors were also recorded. A comparative group of age-matched healthy volunteers with NSS were recruited from the community in response to public advertisements. These individuals were not clinic patients and had no dermatologic or systemic conditions. All volunteers with NSS underwent full clinical examination and laboratory screening and were included only if they met all inclusion criteria and none of the exclusion criteria. NSS status was defined by the absence of clinical skin sensitivity, SS-10 score below 13, and negative LAST responses (< 3).

Participants from both groups were excluded if they met any of the following criteria: (1) active or chronic facial dermatoses; (2) use of systemic or topical antibiotics, antifungals, corticosteroids, isotretinoin, probiotics or antiseptics within 2 weeks before sampling; (3) any significant systemic disease; or (4) history of facial dermatologic procedures (chemical peeling, laser therapy, Intense Pulsed Light (IPL), radiofrequency, High-Intensity Focused Ultrasound (HIFU), or mesotherapy) within the previous 3 months; and pregnancy or lactation. In total, 75 participants were enrolled, including 45 with SS and 30 with NSS.

Study Procedure

All participants provided written informed consent prior to enrollment. The study protocol was approved by the Institutional Review Board of the University of Medicine and Pharmacy at Ho Chi Minh City (*382/HĐĐĐ-ĐHYD, 22/03/2023*). After completing the SS-10 questionnaire, participants from both groups underwent the LAST.

Steps of the LAST

A cotton pad moistened with 10% lactic acid solution was gently rubbed onto one cheek, while another soaked with phosphate-buffered saline (PBS) was applied to the opposite side as a control. Participants rated unpleasant sensations (pain, burning, itching, tingling) on a 0–3 scale (0, none; 1, mild; 2, moderate; 3, severe) at 30 s, 2.5 min, and 5 min after application. The LAST score at each timepoint was defined as the difference between the lactic acid and PBS sides, and the highest score was recorded. A combined scores ≥ 3 at 2.5 min and 5 min indicated a positive LAST.

Afterward, participants underwent microbiome sampling and skin parameter measurements. They were instructed to refrain from applying any topical products (moisturizers, cosmetics, sunscreens) for at least 24 h before sampling and to cleanse the face with plain water only during this period. All procedures were performed in a controlled environment (22 ± 2 °C; 50% ± 10% relative humidity).

Sample Collection

Skin scraping was used to collect microbiome samples from the entire facial surface (forehead, temples, nose, chin, medial and lateral cheeks, jaw) under sterile conditions to minimize external contamination.

During sampling, one hand was used to gently stretch and stabilize the skin, while the other held a sterile no. 10 surgical blade (Doctor™, India) positioned at a 15–30° angle. Using light, repeated strokes, the operator gently scraped the superficial layer of the skin. The collected material was transferred from the blade onto a PBS-moistened sterile cotton swab. When sufficient material had accumulated, the swab head was detached and placed into a sterile 15 mL Falcon tube containing 3 mL sterile PBS. Four swabs were used to sample the entire face. The tubes were sealed and manually agitated for 30 s to disperse the material, then sealed with parafilm and transported on ice to the Molecular Biomedicine Center, where they were stored at 4 °C for no longer than 3 days before DNA extraction was performed. The extracted DNA samples were subsequently stored at –80 °C.

Assessment of Skin Parameters

After microbiome sampling, participants washed their face and equilibrated for 30 min in a

controlled environment (22 ± 2 °C; 50% ± 10% relative humidity). Skin parameters were measured using the Multi Probe Adapter MPA 6 system (Courage + Khazaka electronic GmbH, Germany), including TEWL (Tewameter TM Hex, g/h/m^2); stratum corneum hydration (Corneometer CM 825, arbitrary units); sebum level (Sebumeter SM 815, 0–350 units); surface pH (Skin pH Meter PH 905); and erythema and melanin indices (Mexameter MX 18, 0–999 units).

DNA Extraction

Bacterial DNA was extracted from all scraped skin samples using a standardized protocol. Each sample was placed in a 15 mL Falcon tube containing 1 mL Depletion Solution and 3 mL PBS, vortexed and centrifuged to collect the pellet. The pellet was resuspended, centrifuged again to remove the supernatant, and the remaining 200 µL was retained. DNA extraction was performed with the HostZERO™ Microbial DNA Kit (Zymo Research) with minor modifications: the filtration step was repeated three times, incubation was extended to 10 min, and 20 µL of filtrate was applied to the column, followed by an additional 30 min incubation, and centrifugation at 10,000 × g for 1 min to elute DNA.

Final DNA concentration was quantified using the Qubit™ 4 Fluorometer with the High Sensitivity dsDNA Assay Kit (Thermo Fisher Scientific) following the manufacturer's instructions.

16S rRNA Gene Amplification and Sequencing

The V3-V4 regions of bacterial 16S rRNA gene were amplified using primers 341F (5′-CCTACG GGAGGCAGCAG-3′) and 806R (5′-GGACTA CHVGGGTWTCTAAT-3′). Polymerase chain reaction (PCR) conditions included an initial denaturation at 95 °C for 10 min, followed by 42 cycles of 95 °C for 30 s, 55 °C for 30 s, and 72 °C for 3 min. Amplicons were prepared as 2 × 300 bp libraries using the Quick-16S Plus NGS Library Prep Kit (D6421, Zymo Research, USA) and sequenced on the Illumina Miseq® Dx platform.

To monitor for potential background contamination, negative controls were incorporated at multiple stages of the workflow. A sterile PBS-moistened swab processed through DNA extraction, 16S amplification, and library preparation in parallel with the clinical samples did not generate a detectable library or sequencing reads. PCR no-template controls likewise produced no amplicons or reads, indicating the absence of reagent- or workflow-derived contamination.

Sequencing data have been deposited in the NCBI BioProject database under accession number PRJNA1321538.

Data Processing and Skin Microbiome Analysis

Raw sequencing reads were quality-checked using FastQC (v0.11.9) [33] and trimmed with cutadapt (v4.9) to remove adapters, primers, and low-quality bases ($Q < 30$; length < 70 bp) [34]. High-quality paired-end reads were processed in DADA2 [35] to infer amplicon sequence variants (ASVs). Error models were trained with pooled-sample approach (pool = TRUE), reads were merged, chimeras removed, and an ASV table generated.

Taxonomy was assigned using the Naïve Bayesian Classifier [36], against the SILVA v138.1 database [37] with an 80% confidence threshold. A maximum-likelihood phylogenetic tree was reconstructed under the GTR + G + I model using the phangorn package [38]. All outputs were integrated into a phyloseq object [39] for analyses of diversity, community composition, and statistical testing.

Statistical Analysis and Data Visualization

Comparisons of skin parameters between NSS and SS groups, stratified by sex and age, were performed using the Wilcoxon rank-sum test. Alpha diversity was estimated with the Shannon index (diversity) and Chao1 richness, and group differences were tested using the Wilcoxon test.

For beta diversity analysis, raw read counts were normalized to the centered log-ratio (CLR) transformation (after adding a pseudo-count of 1) addressing the compositional nature of microbiome data. Subsequently, Bray–Curtis dissimilarity was computed, visualized by principal coordinates analysis (PCoA), and tested for significance with permutational multivariate analysis of variance (PERMANOVA) (adonis2, vegan package). Differential abundance analysis was conducted using ANCOM-BC [40, 41] to account for data compositionality.

Association between quantitative variables was assessed using Spearman correlation, relating skin parameters to bias-corrected log-transformed microbial data. For group-wise microbial comparisons, the Wilcoxon test was used for two groups (e.g., presence versus absence of clinical symptoms), and one-way ANOVA for comparisons across three or more symptom-onset groups. To ensure statistical robustness, only groups with a sample size greater than three were included in the analysis.

All analyses were performed in R (v4.x) with data visualization using the ggplot2 package [42] and ComplexHeatmap [43]. False Discovery Rate (FDR) < 0.05 was considered statistically significant after *p*-value correction.

RESULTS

The Skin Characteristics of the Studied Subjects

Participants were classified into NSS ($n = 30$) and SS ($n = 45$) groups on the basis of 10% LAST and SS-10 criteria. The NSS group included 24 female patients and 6 male patients (mean age:

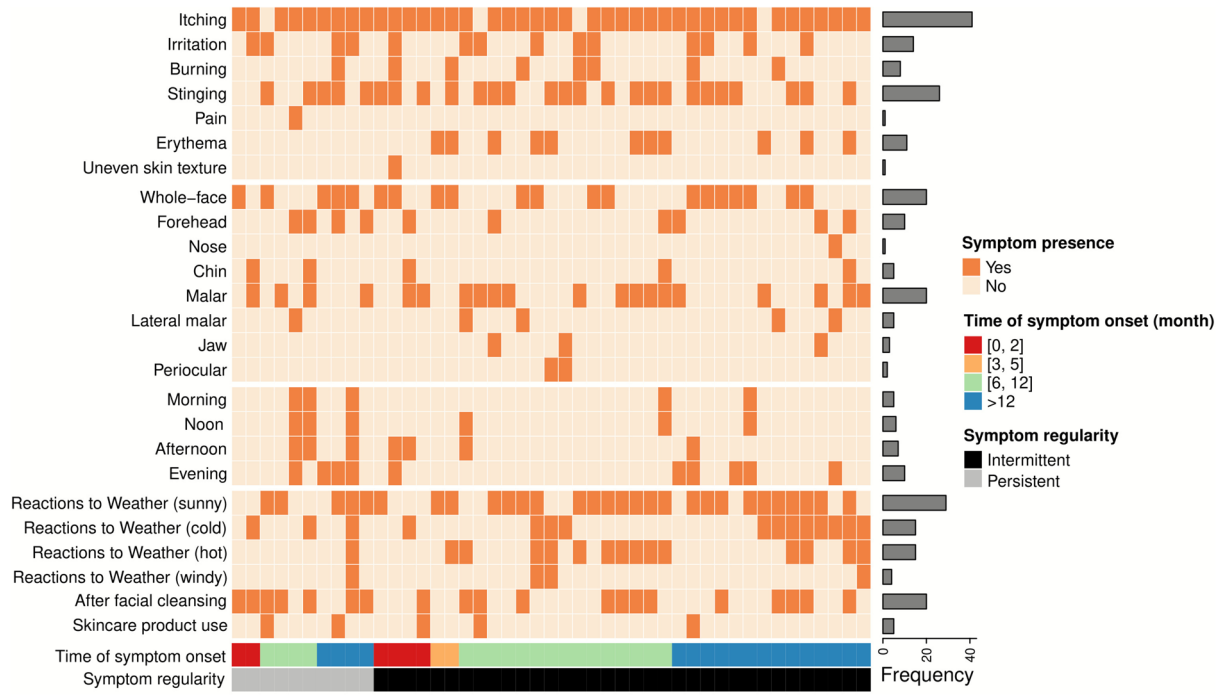

Fig. 1 Comprehensive clinical profile of participants with sensitive skin (SS) illustrating symptom distribution, facial-site involvement, temporal patterns, and trigger factors. Heatmap summarizing the distribution of self-reported symptoms, affected facial regions, daily occurrence times, and environmental or cosmetic triggers among SS participants. Orange indicates symptom presence. Side and bottom annotations represent symptom frequency, time of symptom onset, and symptom regularity. Erythema and stinging were the most frequent symptoms, mainly affecting malar and jaw regions, with weather and cleansing as common triggers

33.7 ± 8.84 years), while the SS group comprised 38 female patients and 7 male patients (mean age: 31.47 ± 7.48 years).

Figure 1 summarizes the clinical characteristics of participants with SS. Itching was the most frequent symptom (91.1%), followed by stinging (57.8%) and irritation (31.1%). Erythema (24.4%) and burning (17.8%) were less common, whereas pain and uneven skin texture were rare (2.2% each). Symptoms predominantly affected the malar region (44.4%) and the whole face (42.2%), and less often in the forehead (22.2%), lateral malar and chin (11.1% each), jaw (6.7%), periocular region (4.4%), and nose

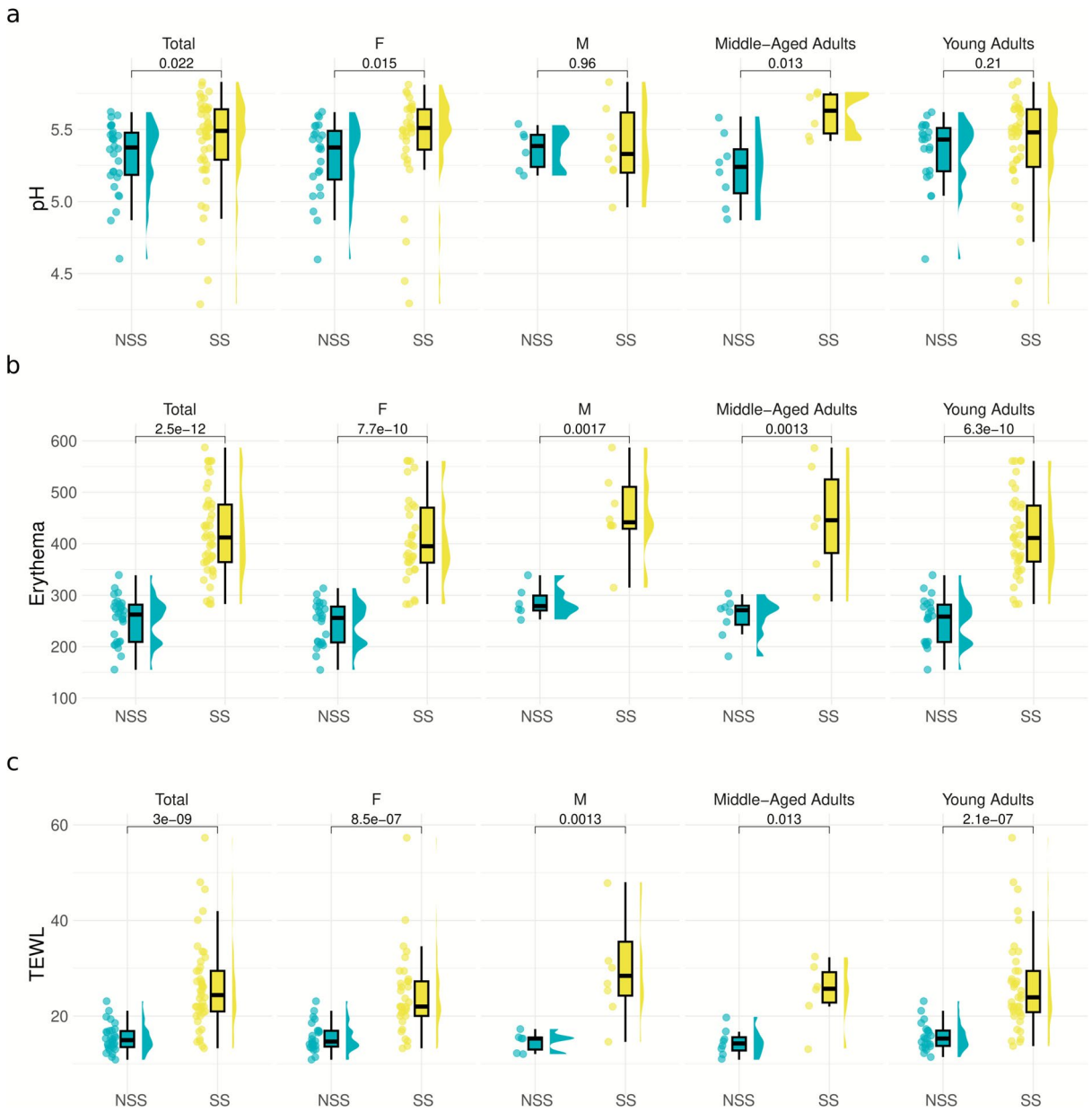

Fig. 2 Comparison of biophysical skin parameters between nonsensitive skin (NSS) and SS groups across sex and age categories. **a** pH, **b** erythema, and **c** transepidermal water loss (TEWL). SS showed significantly higher pH, erythema, and TEWL values, especially in female patients and middle-aged adults

(2.2%). Symptom occurrence varied throughout the day, most often in the evening (22.2%), followed by the afternoon (15.6%), noon (13.3%), and morning (11.1%). Environment triggers were frequent, including sun exposure (64.4%), cold and heat (each 33.3%), and wind (8.9%). Symptoms were also reported after facial cleansing (44.4%) and skincare product use (11.1%). Most participants experienced intermittent symptoms (77.8%), while 22.2% reported persistent discomfort. Regarding onset, 42.2% developed symptoms between 6 and 12 months, and 40.0% beyond 12 months. Early onset was less common, reported in 13.3% within the first 2 months and 4.4% within 3 and 5 months.

Skin parameter analysis revealed significant differences in pH, erythema, and TEWL between groups ($p<0.05$, Fig. 2), whereas sebum, hydration, and melanin showed no differences ($p>0.05$, Fig. S1). Elevated pH was observed in female participants and middle-aged participants with SS (Fig. 2a), while erythema and TEWL were significantly higher in the SS across all sex and age subgroups (Figs. 2b, c).

Microbiome Profiles of SS and NSS

16S rRNA V3-V4 sequencing was performed to compare facial microbiome composition between NSS and SS groups. In the NSS group, sequencing yielded an average of 109,310 reads (SD 67,627), with read counts ranging from 16,005 to 351,775. In the SS group, sequencing generated a mean of 111,941 reads (SD 41,633), with read counts ranging from 12,770 to 225,129 reads. After denoising, a total of 988 bacterial ASVs were retained across all samples. All samples exceeded the minimum sequencing depth requirement, and no samples were excluded due to low read counts.

The Shannon index was 0.57 ± 0.56 in SS and 0.53 ± 0.39 in NSS, while Chao1 richness estimates were 22.66 ± 17.03 and 18.78 ± 14.55, respectively. No significant differences were detected in alpha diversity (Shannon, Chao1, Figs. 3a, b) or beta diversity (Bray–Cutis PCoA, Fig. 3c). Nevertheless, the SS group exhibited a higher number of detected genera (115) than the NSS group (92) (Fig. 3d).

Taxonomic profiling revealed that both groups were dominated by three phyla: *Proteobacteria*, *Firmicutes*, and *Actinobacteriota*, which together accounted for the majority of sequence reads (Fig. 4, S2). At the family level, *Enterobacteriaceae* was identified as the most abundant, comprising seven genera and representing the largest proportion in both groups, followed by *Lactobacillaceae* with six genera (Figs. S2, S3).

Sphingomonadaceae, *Moraxellaceae*, and *Acetobacteraceae* each contained five genera, indicating a comparable level of taxonomic diversity within these lineages (Figs. S2, S3). Although *Staphylococcaceae* was identified as one of the less abundant families overall, the genus *Staphylococcus* remained the most prevalent taxon, occurring as the dominant genus in 97.3% of all samples (Fig. S3), underscoring its ubiquitous presence of *Staphylococcus* across both SS and NSS microbiomes despite compositional differences.

Differences in Taxonomic Composition between SS and NSS

Although alpha and beta diversity metrics did not differ significantly between the NSS and SS groups (Fig. 2), differential abundance analysis using ANCOM-BC identified 53 genera as differentially abundant (FDR<0.05). Among these, 32 genera were enriched and 21 were depleted in SS (Fig. 5). These findings suggest that specific microbial genera respond differently between the two groups.

Two Gram-negative genera, *Peredibacter* and *Enterobacter*, exhibited the highest alternative log fold changes (logFC) of 4.52 and 3.43, respectively, followed by the Gram-positive genus *Marmoricola* with a log FC of 3.04 (Figs. 5a, b). *Staphylococcus* also exhibited a modest positive logFC of 0.60, consistent with its overall high relative abundance (Fig. 5a, b). In contrast, *Streptococcus*, *Escherichia-Shigella*, and *Weissella* showed the largest reductions in SS,

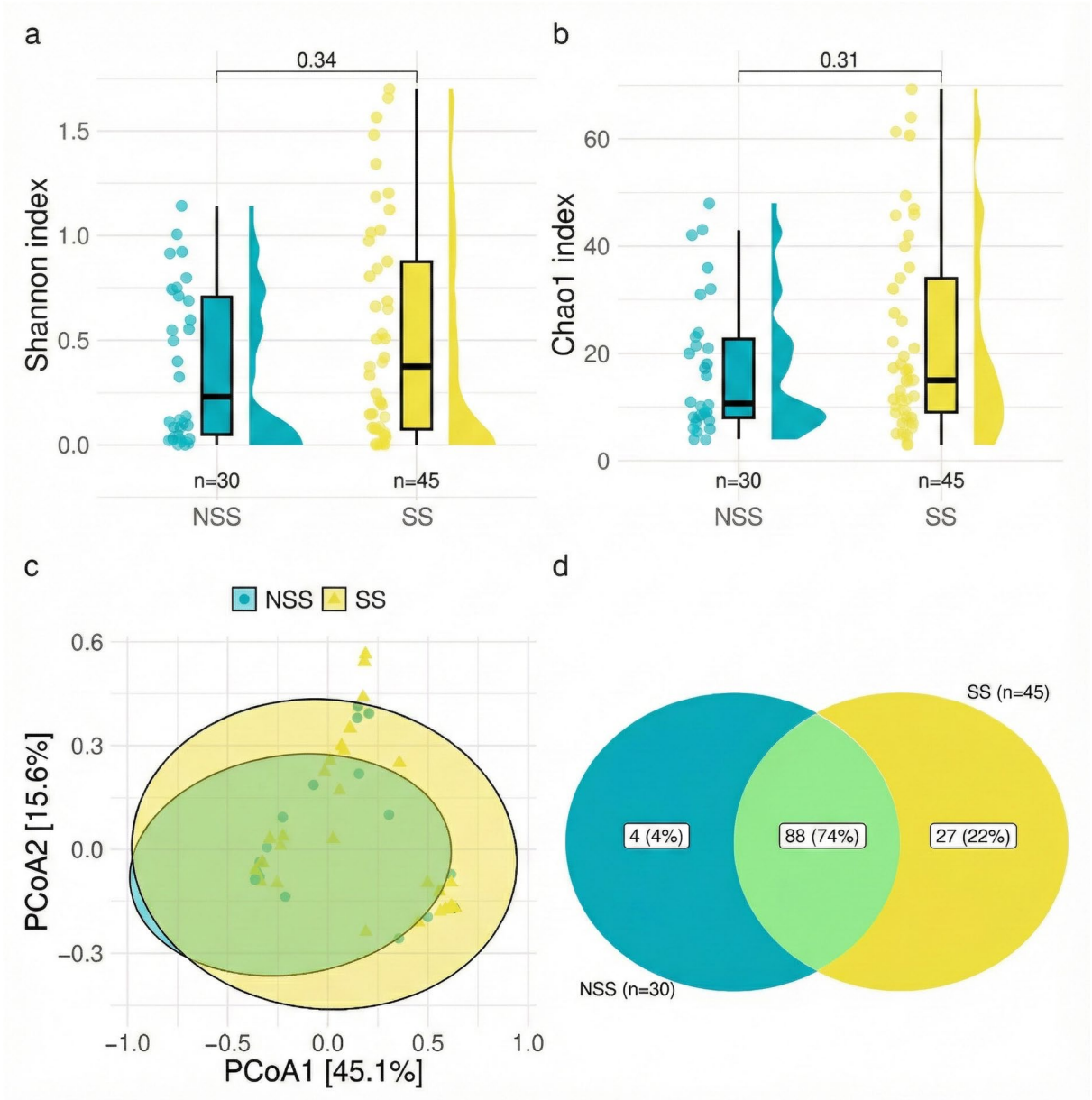

Fig. 3 Overall comparison of bacterial community structure between NSS and SS groups. **a** Shannon and **b** Chao1 indices show no significant difference in α-diversity between NSS and SS. **c** PcoA analysis shows partial overlap of community structure. **d** Venn diagram displays shared and unique genera between groups

with logFC values of −5.06, −3.95, and −2.36, respectively. *Microvirga*, *Craurococcus-Caldovatus*, and *Cutibacterium* showed only minor changes, with logFC values of −0.47, −0.55, and −0.63, respectively (Fig. 5).

Correlation between Taxonomic Composition and Skin Parameters

Spearman correlation analysis was performed to examine associations between bacterial abundance and skin parameters (Table 1).

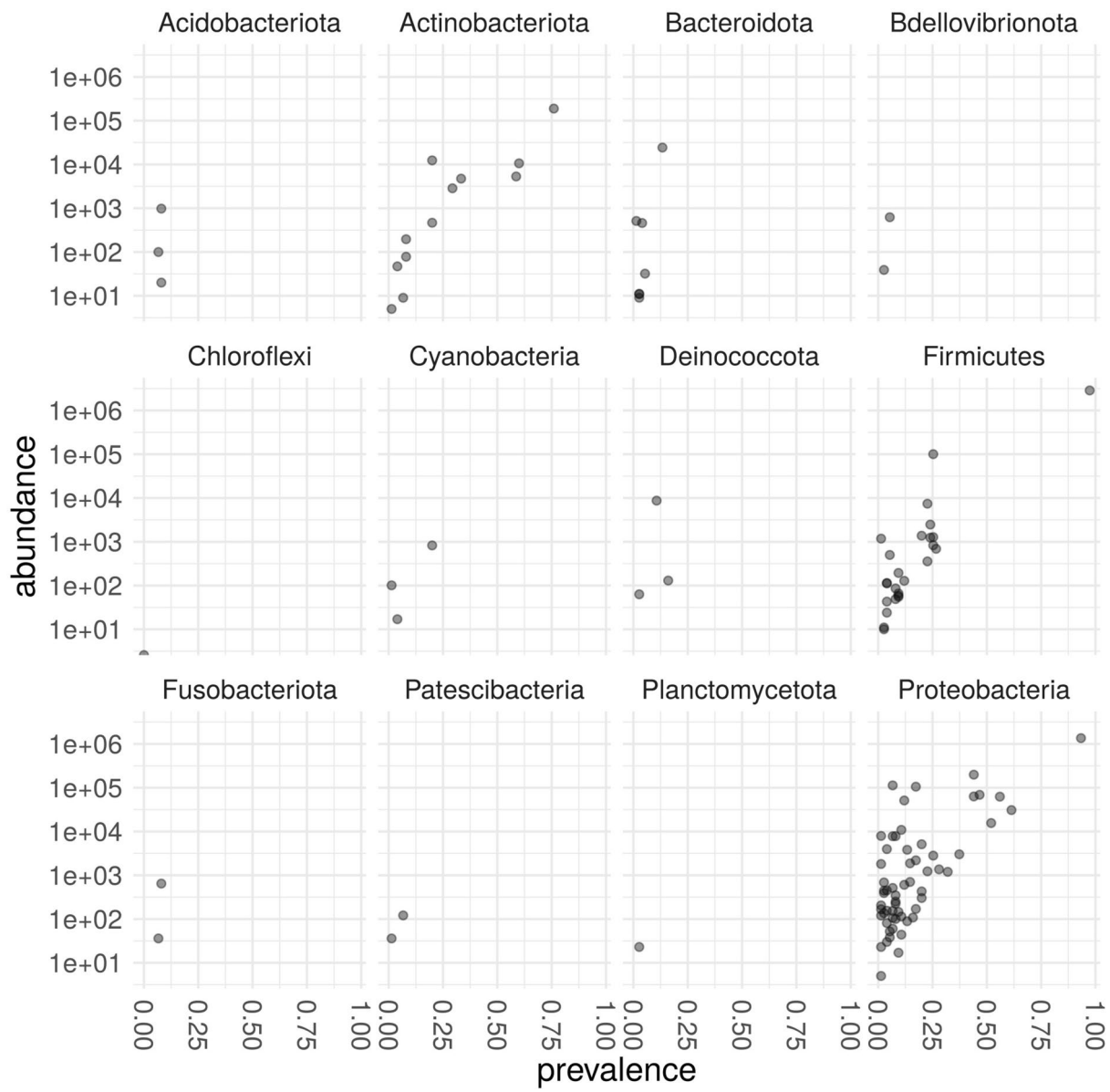

Fig. 4 Prevalence and abundance distribution of bacterial phyla across all analyzed skin samples. *Actinobacteriota*, *Firmicutes*, and *Proteobacteria* dominated the facial skin microbiome

Several genera exhibited significant correlations with sebum level. The strongest negative association was observed for *Marmoricola* ($\rho = -0.34$, FDR = 0.011), followed by *Burkholderia-Caballeronia-Paraburkholderia* ($\rho = -0.28$) and *Craurococcus-Caldovatus* ($\rho = -0.26$). In contrast, *Pseudoxanthomonas* was the only genus showing a significant positive correlation with sebum ($\rho = 0.33$, FDR = 0.015).

Correlations with skin pH were predominantly negative. *Clostridium sensu stricto 1* showed the strongest inverse association ($\rho = -0.38$, FDR = 0.005), followed by *Pluralibacter* ($\rho = -0.29$), *Enterococcus*, *Leptotrichia*, and

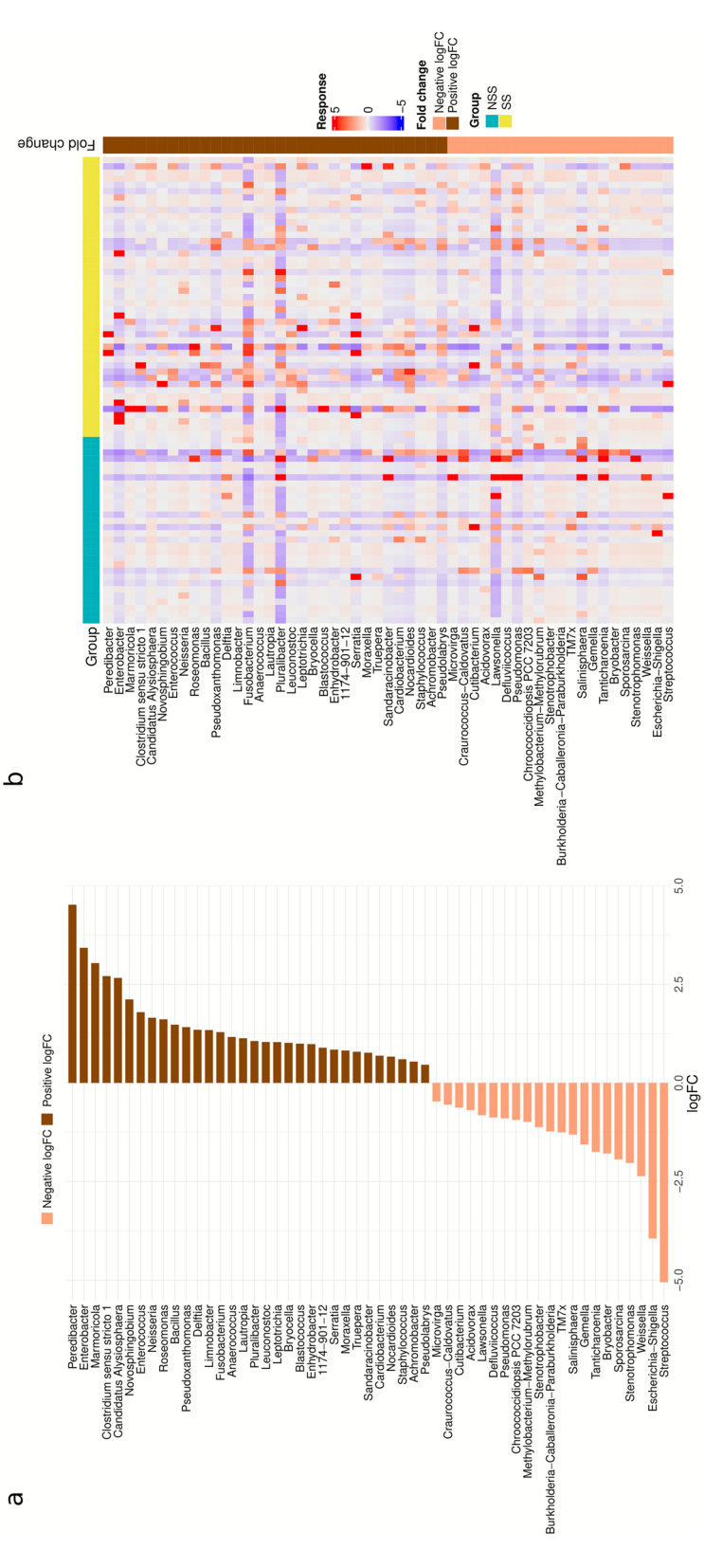

Fig. 5 Differential abundance of bacterial genera between NSS and SS groups. **a** Log fold-change (logFC) values indicate genera enriched or depleted in SS relative to NSS. **b** Heatmap of log transformed abundance values for each genus across samples. *SS* sensitive skin; *NSS* nonsensitive skin

Table 1 Spearman correlation of significant bacteria genera with clinical skin parameters

Genus	Factor	FDR	ρ
Marmoricola	Sebum	0.011	−0.34
Craurococcus-Caldovatus		0.045	−0.26
Burkholderia-Caballeronia-Paraburkholderia		0.034	−0.28
Pseudoxanthomonas		0.015	0.33
Pluralibacter	pH	0.027	−0.29
Clostridium sensu stricto 1		0.005	−0.38
Leptotrichia		0.050	−0.25
Moraxella		0.049	−0.25
Enterococcus		0.034	−0.27
Enterobacter		0.040	0.26
Pseudomonas	Erythema	0.014	−0.33
Craurococcus-Caldovatus		0.022	−0.30
Tanticharoenia		0.028	−0.29
Gemella		0.035	−0.27
Staphylococcus		0.008	−0.36
Lawsonella	TEWL	0.015	−0.32
Streptococcus		0.009	0.35
Serratia		0.006	0.37
Cutibacterium		0.042	0.26
Peredibacter		0.046	0.25
Bryobacter		0.025	0.29
Candidatus Alysiosphaera		0.019	0.31
Chroococcidiopsis PCC 7203		0.013	0.33
Delftia		0.035	0.27
Acidovorax		0.040	0.26
Neisseria		0.044	0.26
Stenotrophobacter		0.048	0.25

Moraxella. *Enterobacter* was the only genus displaying a significant positive correlation with skin pH (ρ = 0.26, FDR = 0.04).

For erythema, all significant associations were negative. The strongest correlations were observed for *Staphylococcus* (ρ = –0.36, FDR = 0.008) and *Pseudomonas* (ρ = –0.33), followed by *Craurococcus-Caldovatus* (ρ = –0.30), *Tanticharoenia*, and *Gemella*.

In contrast, correlations with TEWL were predominantly positive. *Serratia* showed the strongest association (ρ = 0.37, FDR = 0.006), followed by *Streptococcus* (ρ = 0.35). Additional genera positively correlated with TEWL included *Chroococcidiopsis PCC 7203*, *Candidatus Alysiosphaera*, *Bryobacter*, *Delftia*, *Acidovorax*, *Neisseria*, *Cutibacterium*, *Stenotrophobacter*, and *Peredibacter*, whereas *Lawsonella* was the only genus showing a significant negative correlation (ρ = –0.32, FDR = 0.015).

Distinct Microbial Community Profiles Associated with Clinical Outcomes

We then investigated differences in microbial abundance associated with clinical symptoms, facial location, time of day of symptom occurrence, trigger factors, symptom regularity, and time of symptom onset. In total, 37 genera showed differential abundance (Table 2), including 19 associated with clinical symptoms (Table 2A), 16 with facial location (Table 2B), 3 with symptom regularity (Table 2C), and 5 with time of symptom onset (Table 2D).

Several genera were significantly associated with the presence or absence of specific clinical symptoms (Table 2A). The largest number of associations was observed for burning ($n = 8$ present versus $n = 37$ absent), where *Pluralibacter*, *Lawsonella*, *Sphingomonas*, *Pseudomonas*, *Pseudoxanthomonas*, and *Bosea* were significantly more abundant in the symptom-absent group, and *Bryobacter* showed higher abundance in symptom-present individuals. For irritation ($n = 13$ present versus $n = 32$ absent), *Klebsiella*, *Qipengyuania*, and *Pseudomonas* were depleted in symptom-present cases, while *Methylobacterium-Methylorubrum* was enriched. Stinging ($n = 26$ present versus $n = 19$ absent) was associated with increased abundance of *Clostridium sensu stricto 1*, *Leptotrichia*, and *Acidovorax*, whereas *Cardiobacterium* was reduced. In itching ($n = 40$

Table 2 Differential abundance analysis of bacterial genera associated with (A) clinical symptoms, (B) anatomic locations of clinical symptoms, (C) symptom regularity, and (D) time of symptom onset

(A) Clinical symptoms						
Genus	**Symptoms**	**FDR**	**No. sample**		**Average log (abn)**	
			With	**Without**	**With**	**Without**
Pluralibacter	Burning	0.001	8	37	−0.95	0.63
Lawsonella		0.039			−0.68	0.01
Sphingomonas		0.001			−0.58	0.18
Pseudomonas		0.007			−0.43	0.19
Pseudoxanthomonas		0.002			−0.43	0.39
Bosea		0.007			−0.57	0.14
Bryobacter		0.025			0.28	−0.07
Klebsiella	Irritation	0.037	13	32	−0.44	0.61
Qipengyuania		0.006			−0.74	0.19
Pseudomonas		0.012			−0.47	0.30
Methylobacterium-Methylorubrum		0.034			0.65	−0.10
Clostridium sensu stricto 1	Stinging	0.049	26	19	0.63	−0.31
Leptotrichia		0.014			0.52	−0.27
Cardiobacterium		0.028			−0.15	0.55
Acidovorax		0.038			0.20	−0.11
Pseudomonas	Itching	0.022	40	5	0.17	−0.64
Kocuria	Erythema	0.041	10	35	− 0.52	0.23
Defluviicoccus		0.003			0.14	− 0.23
Acinetobacter		0.030			0.32	−0.09
Chryseobacterium		0.015			−0.15	0.28
Acidovorax		0.029			0.26	0.02
Burkholderia-Caballeronia-Paraburkholderia		0.001			0.33	−0.02

Table 2 continued

(B) Anatomic locations of clinical symptoms						
Genus	**Location**	**FDR**	**No. sample**		**Average log (abn)**	
			With	**Without**	**With**	**Without**
Pseudoclavibacter	Malar	0.048	20	25	1.05	−1.05
Enterobacter		0.049			1.24	−0.48
Tanticharoenia		0.015			−0.46	0.24
Microvirga		0.050			−0.20	0.18
Deinococcus		0.031			−0.09	0.46
Gemella		0.009			−0.21	0.21
Staphylococcus		0.022			−0.27	0.32
Enterobacter	Lateral malar	0.031	5	40	0.61	−0.61
Clostridium sensu stricto 1		0.042			0.32	−0.46
Pseudoxanthomonas		0.001			0.34	−0.57
Enterobacter	Chin	0.043	5	40	0.61	−0.59
Corynebacterium		0.031			0.35	−0.58
Allorhizobium-Neorhizobium-Pararhizobium-Rhizobium		< 0.001			0.43	−1.06
Pseudoclavibacter	Forehead	0.001	10	35	0.69	−1.90
Enterobacter		0.013			0.84	−0.82
Gemella		0.025			−0.12	0.30
Enterobacter	Whole face	0.027	19	26	−0.57	1.91
Craurococcus-Caldovatus		0.002			0.33	−0.46
Luteimonas		0.013			0.28	−0.32
Cardiobacterium		0.043			0.40	−0.19

(C) Symptom regularity						
Genus	**Factor**	**FDR**	**No. samples**		**Average log (abn)**	
			Intermittent	**Persistent**	**Persistent**	**Intermittent**
Klebsiella	Regularity	0.032	35	10	−0.50	0.54
Novosphingobium		0.031			−0.15	0.39
Cloacibacterium		0.033			−0.21	0.32

Table 2 continued

(D) Time of symptom onset										
Genus	**Factor**	**FDR**	**No. samples**				**Average log (abn)**			
			[0, 2]	**[3, 6]**	**[6, 12]**	**> 12**	**[0, 2]**	**[3, 6]**	**[6, 12]**	**> 12**
Enterobacter	Time onset	0.043	6	2	19	18	2.60	4.76	−0.36	0.17
Kosakonia		0.037					−0.21	4.41	0.65	−0.56
Rothia		0.029					0.61	3.58	−0.55	−0.33
Craurococcus-Caldovatus		0.027					−0.15	−0.33	0.47	−0.42
Chryseobacterium		0.035					−0.13	−0.20	−0.08	0.62

present versus $n=5$ absent), *Pseudomonas* showed significantly higher abundance in symptom-present individuals. Finally, erythema ($n=10$ present versus $n=35$ absent) was associated with increased abundance of *Defluviicoccus*, *Acinetobacter*, *Acidovorax*, and *Burkholderia-Caballeronia-Paraburkholderia*, alongside reduced abundance of *Kocuria* and *Chryseobacterium*, indicating symptom-specific microbial shifts.

Anatomical location-specific analyses demonstrated that microbial composition varied according to the facial distribution of sensitive skin manifestations (Table 2B). In the malar region ($n=20$), *Pseudoclavibacter* and *Enterobacter* were significantly enriched, while several genera, including *Tanticharoenia*, *Microvirga*, *Deinococcus*, *Gemella*, and *Staphylococcus*, were reduced compared with individuals without malar involvement ($n=25$). The lateral malar region ($n=5$) was characterized by enrichment of *Enterobacter*, *Clostridium sensu stricto 1*, and *Pseudoxanthomonas* relative to unaffected sites ($n=40$). On the chin ($n=5$), *Enterobacter*, *Corynebacterium*, and *Allorhizobium-Neorhizobium-Pararhizobium-Rhizobium* were consistently more abundant than in participants without chin symptoms ($n=40$). Forehead involvement ($n=10$) was associated with increased abundance of *Pseudoclavibacter* and *Enterobacter*, accompanied by reduced *Gemella* compared with asymptomatic individuals ($n=35$). In contrast, whole-face involvement ($n=19$) showed enrichment of *Craurococcus-Caldovatus*, *Luteimonas*, and *Cardiobacterium*, whereas *Enterobacter* exhibited lower relative abundance than in those without whole-face symptoms ($n=26$). These findings indicate that the skin microbiome exhibits distinct, location-dependent compositional shifts associated with the anatomical distribution of sensitive skin symptoms.

A significant association was also observed with symptom regularity (intermittent versus persistent). *Klebsiella*, *Novosphingobium*, and *Cloacibacterium* showed higher relative abundance in individuals with intermittent symptoms ($n=10$) compared with those with persistent symptoms ($n=35$), suggesting a higher relative abundance of these taxa in individuals with intermittent symptoms.

Analysis of microbial community structure further revealed associations with time of symptom onset, as assessed by one-way ANOVA (Table 2D). Five genera, including *Enterobacter*, *Kosakonia*, *Rothia*, *Craurococcus-Caldovatus*, and *Chryseobacterium*, showed significant differences in bias-corrected log abundance across the four onset categories (0–2, 3–6, 6–12, and >12 months). *Enterobacter*, *Kosakonia*, and *Rothia* exhibited their highest average log abundance in the 3–6-month onset group, whereas *Craurococcus-Caldovatus* showed relatively higher abundance in the 6–12-month group. In contrast, *Chryseobacterium* reached its highest abundance in individuals with symptom duration exceeding 12 months. These patterns suggest that symptom onset duration is associated with distinct microbial profiles.

DISCUSSION

The present study provides new insights into the clinical and microbial characteristics of SS in a Vietnamese cohort by integrating objective biophysical parameters with 16S rRNA sequencing-based microbiome profiling. Our findings demonstrate alterations in skin physiological parameters, distinct microbial patterns, and associations between specific bacterial taxa and clinical features, contributing to a more integrated characterization of the SS phenotype in an underrepresented population.

Participants with SS exhibited significantly higher TEWL and erythema index across all subgroups, while elevated pH was particularly pronounced in female patients and middle-aged adults (Fig. 2). These results are consistent with prior studies reporting impaired barrier function and increased skin reactivity in SS. TEWL elevation has been widely reported as an indicator of stratum corneum dysfunction [10, 14], whereas erythema is commonly interpreted as reflecting increased neurovascular responsiveness [44].

In contrast, parameters such as sebum, hydration, and melanin index showed no significant differences between SS and NSS groups (Figure S1), consistent with prior observations that biophysical changes in SS are often subtle and localized rather than systemic [45, 46]. The elevated surface pH observed in this study is partially aligned with earlier reports, though findings remain inconsistent across cohorts [45, 47, 48]. Such discrepancies may reflect methodological heterogeneity or demographic variation, as skin pH varies with ethnicity, gender, and hormonal status [49]. The elevation observed among female patients here may reflect sex-related differences in skin barrier biochemistry, warranting further exploration.

Previous studies have emphasized pH and TEWL vary by anatomical site and season [50], and that SS presentations differ across geographic regions [51]. Collectively, these findings reinforce the heterogeneity of SS and suggest that demographic and environmental context may contribute to observed differences across populations.

At the community level, both SS and NSS groups exhibited a canonical skin microbiome dominated by *Actinobacteriota*, *Firmicutes*, and *Proteobacteria* (Fig. 4), consistent with seminal descriptions of the human skin microbiota [20, 23] and with reports from East Asian cohorts [45, 46, 48]. These three phyla represent the core commensal population across sebaceous, moist, and dry skin sites and collectively shape the cutaneous ecological balance. Within this framework, *Staphylococcus* was the most prevalent genus, detected in more than 97% of samples (Fig. S3), in line with its role as a common skin commensal [21, 52]. However, the functional implications of *Staphylococcus* are strain-dependent while *S. epidermidis* contributes to antimicrobial defense and *S. aureus* has been associated with barrier dysfunction [52]. In the current study, *Staphylococcus* remained highly prevalent but not dominant in relative abundance, which may reflect subtle community variation.

Although α- and β-diversity metrics did not differ significantly between the SS and NSS groups (Figs. 3a-c), differential abundance analysis (ANCOM-BC, FDR < 0.05) revealed 53 genera with significant shifts, suggesting compositional remodeling rather than an overall reduction in community diversity. Among the taxa enriched in SS, *Enterobacter* and *Peredibacter* were notable (Fig. 5a, b). Certain Gram-negative genera, such as *Enterobacter*, have been linked to barrier perturbation and cutaneous reactivity in prior studies, whereas the presence of *Peredibacter* may reflect altered skin ecological conditions. However, mechanistic interpretations remain speculative in the absence of species- or strain-level data. *Marmoricola*, an actinobacterium of uncertain function, was also increased and warrants further investigation.

Conversely, *Streptococcus*, *Escherichia-Shigella*, and *Weissella* were significantly depleted in SS (Fig. 5). These genera are commonly regarded as part of the normal skin microbiota, and their reduction has been noted in some prior studies of altered barrier state [53]. A lower relative *Cutibacterium* abundance, a typical inhabitant of sebaceous regions, may likewise reflect changes in the local microenvironment. Notably,

previous studies have reported inconsistent patterns for *Staphylococcus* in SS [46, 48, 54], suggesting that regional or methodological factors may modulate this genus' relative abundance.

Interestingly, *Neisseria* also differed between SS and NSS groups (Fig. 5). Although typically a mucosal commensal, *Neisseria* species have been reported in some contexts to contribute to colonization resistance [55, 56]. Whether a similar role exists on facial skin remains uncertain, but this variability highlights the complexity of microbial interactions in SS.

The enrichment of Gram-negative taxa and depletion of commensals in our Vietnamese cohort collectively suggest a pattern of altered microbial balance in SS. This pattern differs from the dysbiosis typically described in atopic dermatitis or rosacea, where *S. aureus* or *Demodex*-associated bacteria dominate [27, 57]. These distinctions may indicate that SS reflects a more subtle microbial shift.

These findings indicate that the SS phenotype is characterized by subtle microbial shifts, raising the possibility of interactions between microbial composition and local skin physiology. Further studies integrating metabolomics and transcriptomics will be valuable to clarify whether and to what extent Gram-negative enrichment relates to sensory and vascular reactivity in SS.

Our study further explores the interface between microbial abundance and skin physiological parameters, showing that sebum level, skin pH, erythema index, and TEWL were associated with genus-level microbiome variation. Although TEWL was significantly elevated in SS, its associations involved multiple taxa rather than a single dominant genus, suggesting that barrier disruption in SS may reflect a permissive ecological state and may also involve intrinsic epidermal features such as tight-junction integrity and lipid composition [14, 58].

Among the identified taxa, *Enterobacter* showed a positive correlation with skin pH ($\rho = 0.26$, FDR = 0.040), suggesting that shifts in certain Gram-negative genera may co-occur with changes in surface acidity. In contrast, *Pluralibacter*, *Clostridium sensu stricto 1*, *Leptotrichia*, *Moraxella*, and *Enterococcus* were negatively correlated with pH, consistent with preferential persistence of some taxa under more acidic skin conditions. These associations should be interpreted as concurrent ecological states.

All significant correlations with erythema were negative, with the strongest inverse associations observed for *Staphylococcus* ($\rho = -0.36$) and *Pseudomonas* ($\rho = -0.33$), followed by *Craurococcus-Caldovatus*, *Tanticharoenia*, and *Gemella*. This pattern indicates that increased erythema is accompanied by reduced relative abundance of several common skin-associated genera.

Sebum levels were predominantly negatively correlated with *Marmoricola*, *Craurococcus-Caldovatus*, and *Burkholderia-Caballeronia-Paraburkholderia*, whereas *Pseudoxanthomonas* was the only genus showing a positive association, suggesting selective ecological responses to lipid-rich environments.

In contrast, TEWL showed predominantly positive correlations with a broad range of genera, including *Serratia*, *Streptococcus*, *Cutibacterium*, *Peredibacter*, *Neisseria*, *Delftia*, and *Acidovorax*, while *Lawsonella* was negatively associated. TEWL was associated with multiple genera, indicating that barrier impairment in SS is linked to widespread microbial changes.

These findings extend earlier work by Hillion et al. [32], which emphasized *Staphylococcus epidermidis* imbalance in SS by demonstrating that multiple Gram-negative genera, including members of the *Enterobacteriaceae*, are also associated with physiological parameters in SS. Although species-level evidence remains limited, previous reports of facial microbiome shifts involving *Proteobacteria* and *Neisseriaceae* are consistent with an association between Gram-negative taxa and barrier-reactive skin states [45, 48, 59–61].

Taken together, the present results indicate that microbial alterations in SS vary according to physiological parameters, and do not exhibit a uniform *Staphylococcus*-centered dysbiosis as observed in inflammatory dermatoses such as atopic dermatitis [25, 50]. Despite dominance of *Proteobacteria*, *Firmicutes*, and *Actinobacteriota*, consistent with canonical skin microbiome profiles [20, 23], the observed correlations highlight

the ecological complexity underlying the SS phenotype.

Detailed analysis of symptom-specific microbial patterns revealed distinct associations between bacterial genera and sensory or vascular manifestations of SS (Table 2A). In individuals reporting irritation, *Klebsiella*, *Qipengyuania*, and *Pseudomonas* were significantly depleted, whereas *Methylobacterium-Methylorubrum* showed increased abundance, suggesting selective shifts rather than generalized overgrowth of Gram-negative taxa. Stinging symptoms were associated with higher abundance of *Clostridium sensu stricto 1*, *Leptotrichia*, and *Acidovorax*, alongside reduced *Cardiobacterium*. These taxa include species capable of fermentative metabolism, which has been proposed to influence local skin pH and sensory perception, although direct functional links remain speculative [44].

Participants reporting burning exhibited reduced abundance of multiple genera, including *Pluralibacter*, *Lawsonella*, *Sphingomonas*, *Pseudomonas*, *Pseudoxanthomonas*, and *Bosea*, while *Bryobacter* was relatively enriched, indicating a pattern of commensal depletion rather than pathogen dominance. In contrast, itching was associated with increased abundance of *Pseudomonas*, suggesting that alterations in sebaceous or lipid-associated niches may accompany pruritic symptoms. For erythema, increased abundance of *Acinetobacter*, *Acidovorax*, and *Burkholderia-Caballeronia-Paraburkholderia*, together with reduced *Kocuria* and *Chryseobacterium*,, highlights symptom-specific microbial shifts linked to vascular manifestations.

Marked site-specificity highlights the influence of local cutaneous microenvironments on bacterial community composition in sensitive skin (Table 2B). In the forehead region, enrichment of *Pseudoclavibacter* and *Enterobacter*, together with reduced *Gemella*, suggests that this site exhibits a distinct microbial profile compared with unaffected individuals. Similar enrichment of *Pseudoclavibacter* and *Enterobacter*, alongside reduced *Staphylococcus*, was observed in the malar region, indicating shared but location-dependent compositional patterns.

The lateral malar region showed enrichment of *Enterobacter*, *Clostridium sensu stricto 1*, and *Pseudoxanthomonas*, consistent with site-specific ecological variation, although the small sample size warrants cautious interpretation. The chin region was characterized by co-enrichment of *Enterobacter* and the *Allorhizobium-Neorhizobium-Pararhizobium-Rhizobium* group, taxa commonly detected in moist or occluded skin environments. These findings suggest that microbial alterations associated with SS vary according to facial location, reflecting heterogeneous and locally modulated ecological conditions across the face.

Analyses stratified by symptom regularity revealed distinct microbial associations between intermittent and persistent presentations (Table 2C). Individuals with intermittent symptoms showed higher relative abundance of *Klebsiella*, *Novosphingobium*, and *Cloacibacterium* compared with those with persistent symptoms. Although the functional significance of these associations remains unclear, the observed differences suggest that symptom regularity may be accompanied by distinct ecological states of the skin microbiome.

Microbial composition differed according to categories of time since symptom onset (Table 2D). *Enterobacter*, *Kosakonia*, and *Rothia* exhibited higher relative abundance in individuals reporting symptom onset of 3–6 months, whereas *Chryseobacterium* was more abundant in those with symptom duration exceeding 12 months. *Craurococcus-Caldovatus* showed variable abundance across onset categories without a consistent pattern. These findings indicate that symptom-onset duration is associated with distinct microbial profiles.

Limitations

This study has several limitations. The sample size was modest and derived from a single-center Vietnamese cohort, which may limit generalizability across broader populations and environmental contexts. The cross-sectional design precludes causal inference regarding whether microbial shifts precede or follow

barrier impairment. Participants were instructed to follow a standardized presampling skincare protocol to reduce short-term interindividual and environmental variability. Nevertheless, behavioral and environmental exposures such as mask wearing and ultraviolet radiation could not be fully controlled and may have contributed to regional microbial variability. The present report focuses on bacterial community profiling by design; parallel fungal analyses are underway and will be reported separately. Functional and longitudinal studies integrating bacterial and fungal datasets, along with host barrier biomarkers, will be valuable to clarify microbe–host interactions underlying the sensitive skin phenotype.

CONCLUSIONS

This study provides an integrated clinical and microbiome characterization of sensitive skin in a Vietnamese population. Objective skin assessments showed that pH, transepidermal water loss, and erythema were significantly higher in SS compared with NSS, consistent with impaired barrier function and increased skin reactivity. Microbiome profiling showed that although overall bacterial diversity was comparable between groups, several taxa, particularly *Enterobacter* and other context-dependent Gram-negative genera, displayed differential abundance, indicating modest shifts in community composition.

Correlation and spatial analyses further identified symptom- and site-specific microbial patterns, including selective shifts of Gram-negative taxa across vascular and sensory manifestations, commensal depletion in malar regions, and distinct associations of genera such as *Klebsiella*, *Novosphingobium*, *Enterobacter*, and *Chryseobacterium* with symptom regularity and onset categories. These findings suggest that SS may be associated with the interplay of microbial composition, biophysical parameters, and environmental context. This study provides a population-specific microbiome reference for Vietnamese facial skin and offers a basis for future longitudinal and mechanistic investigations in SS.

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Declarations

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