

Review Article

Aging-related skin microbiome in healthy Asian women

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Abstract

The skin, an environment for the microbiome, has different physical, chemical and physiological states depending on the its site and the individuals. Because of these differences, the community and ecosystem of the microbiome are different for each individual. The differences in these microbiome ecosystems are also determined by their genetic properties, such as demographics, gender, age, race, level of hygiene, lifestyle, and physical injuries. Little is known about the association of microbiome and aging in Asian population. This review aim to gather current knowledge on aging-related skin microbiome in Asian women, namely Korean, Chinese and Thai. Changes in microbiome was found to be not only age-related but also ethnicity-associated. Future study with larger sample size is warrant to further elucidate the association of aging and skin microbiome in Asian female population.

Keywords: Skin aging, skin microbiome, Asian women, aesthetics, genetic

Introduction

Human skin is the outermost layer of body protection, which turn out to be inhabited by various kinds of microorganisms, such as bacteria, fungi and viruses, with a concentration of more than 10^7 cells/cm² (Grice, 2020). The microbiome of human skin, apart from functioning as an immune system, produce metabolites that also functions as a skin barrier, anti-aging and anti-inflammatory (Swaney & Kalan, 2021). The skin, which is the environment for the microbiome, has different physical, chemical and physiological states depending on the site and the individuals (Grice, 2020). Because of these differences, the community and ecosystem of the microbiome are different for each individual (Grice et al., 2009). The differences in these microbiome ecosystems are also determined by their genetic properties, such as demographics, gender, age, race, level of hygiene, lifestyle, and physical injuries, and these changes can occur quickly, even within hours (Meadow et al., 2013).

As the skin ages, structural changes and functional characteristics occur in the skin (Ganceviciene et al., 2012). Today, interest in skin care and anti-aging is increasing in society along with increased research on the causes of skin aging (Shibagaki et al., 2017). Several studies have linked the relationship between the skin microbiome and skin aging and it is known that changes in the skin microbiome are accompanied by changes in the individual's skin condition (Kim et al., 2019).

The metabolites produced by microbiome play an important role in host-microorganism interactions, and the production of these metabolites is strongly influenced by the skin environment and host behaviour (Prescott et al., 2017). A study on 71 Chinese subjects showed that skin microbiome changes were influenced by skin site, age, sex and place of residence (Ying et al., 2015). Another study showed that the skin microbiome in Korean women shows different patterns according to age, skin area and occupation (Kim et al., 2020).

With the advancement of cultivation-independent sequencing technology, there is increasing interest in further research on the microbiome with a variety of different

individual backgrounds (Caporaso et al., 2011). The Human Microbiome Project (HMP) has an extensive data collection, producing some of the most informative reports of the skin microbiome using high-throughput sequencing (The Human Microbiome Project Consortium, 2020). However, studies reporting the effect of aging on the skin microbiome are mostly conducted on Western individuals (Hospodsky et al., 2014), leads to little knowledge on the topic among Asian population. Given that racial and geographic differences can affect skin properties, it is only natural that variations in skin properties will have distinct microbiome communities, as seen in every part of the human body (David et al., 2016). This review aim to gather current knowledge on aging-related skin microbiome in Asian women. This review is expected to add on the understanding of the association of skin microbiome and age as well as race.

Characteristics of the skin microbiome at various ages in china

A study on skin microbiome was conducted on 73 Chinese women who were free from cutaneous clutters (Kim et al., 2020). From the tests conducted on a cohort of more mature women (ages 50–60, hereinafter referred to as the 50s–60s group), a total of 36,533 normal combined sequences were generated and compared with those obtained from a previously reported group of 48 women (ages 25–35, hereinafter referred to as the 20s–30s group). Concurring to the taxonomical assignments by Ribosomal Database Extend II classification, the four overwhelming phyla were Proteobacteria (36.4%, mean relative abundance), Bacteroidetes (22.5%), Firmicutes (18.5%) and Actinobacteria (18.5%). The 10 most inexhaustible genera, comprising >57% of the microbiomes, were Cutibacterium, Chryseobacterium, Enhydrobacter, Staphylococcus, Sphingomonas, Bacteroides, Acinetobacter, Corynebacterium, Streptococcus and Neisseria.

Moreover, this research utilized the linear discriminant analysis effect size (LEfSe) method to identify taxonomic biomarkers contributing to age-related variations in skin microbiomes with high stringency (linear discriminant analysis (LDA) >2.5). A total of 58 operational taxonomic units (OTUs) were identified as distinct in either of the two groups: 30 OTUs in the 20s–30s group and 28 OTUs in the 50s–60s group. The LEfSe analysis revealed a significantly higher abundance of the Bacteroidetes and Firmicutes phyla in the 20s–30s group. Among the OTUs associated with Bacteroidetes, those specific to Bacteroides, Alistipes, Prevotella, Porphyromonas, and Sphingobacterium were exclusively found in this age group. Additionally, among the OTUs belonging to Firmicutes, those of Lactobacillus, Aerococcus, Oscillospira, and Ruminococcus were exclusive to this group. In contrast, the Proteobacteria and Actinobacteria phyla were more abundant in the 50s–60s group. Among the OTUs associated with Actinobacteria, those specific to Micrococcus, Corynebacterium, Dermacoccus, and Actinomyces were exclusively found in the older group. Furthermore, among the OTUs belonging to Firmicutes, those of Streptococcus, Lysinibacillus, and Bacillus were prevalent exclusively in this older group.

Aside from its affiliation with skin illnesses and declined aesthetics in humans, skin maturing has been suggested to be associated with changes within the skin microbiome. A study showed that skin microbiome was distinctively different among women aged 21–37 years old and 60–76 years old, suggesting association of age and skin microbiome (Shibagaki et al., 2017). Microbial changes in grown-up skin were generally affected by the chronological and physiological skin maturing related with verbal microscopic organisms. These contrasts are clarified by the skin microbiome arrangement prepare which can be altogether impacted by the urban and living

situations, especially the individual's private environment and lifestyle (Kim et al., 2018).

In addition, a few analysts have endeavoured to explore the association of skin maturing and infection or age-related infections with microbiomes present at particular destinations within the body (e.g. the intestine and oral cavity) (Zapata & Quagliarello, 2016). However, most of these studies examined differences in microbial communities only at the higher taxonomic levels, such as the phylum level, or inferred results for specific microbes or parasites within the context of a particular human disease. A recently conducted skin microbiome study in North American subjects has identified associations between chronological age, skin aging, and specific taxa and found that age is correlated with two commonly coexisting *Corynebacterium* OTUs (Dimitriu et al., 2019). Nevertheless, skin aging indicators, such as wrinkles and pigmentation spots, were linked to age independently of these taxa. The study also reported no association between these taxa and skin aging factors, such as wrinkles and hyperpigmented spots. Although our study did not measure specific skin aging factors, further investigations revealing the relationship between the 20s–30s and 50s–60s groups (or the A-type and Y-type sub-groups) skin microbiomes and skin aging factors would be of great interest.

Aging slowing cellular digestion system over time and the skin will unavoidably display aging-related characteristics such as decreased fibroblast movement and collagen synthesis (Toledano-Macías et al., 2023). Moreover, diminished vascularisation, sweating and sebum discharge cause the skin to dry, suggesting that physiological changes are associated with skin microbiome.

As skin microbiome studies grow, examination on skin parameters such as pH, sebum substance, dampness substance and TEWL have done to clarify the characteristics of skin microbiomes in different subjects related with particular skin illnesses or aging (Dimitriu et al., 2019). Sebum substance and TEWL were found to be diverse between the more youthful and older women, but PCoA investigation gathered by person skin parameters (information not appeared) showed that the age figure portrays the characteristics of the generally skin microbiome way better than any specific skin parameter (Dimitriu et al., 2019).

Characteristics of the skin microbiome at various ages and gender in Korea

A study conducted on 51 individuals from Korea to analyse their dermatological qualities where participants were divided into two groups, younger and older. This study found that the older group demonstrated elevated periorbital wrinkles and the quantity of marks such as moles and UV spots but declined level of moisture. (Kim et al., 2021). The level of moisture content in the skin, known as cheek, along with the presence of periorbital wrinkles and the quantity of marks such as moles and UV spots, are all factors that contribute to identifying an individual as older. Chronological increment in age was related to the clinical appearance of facial wrinkles and facial hyperpigmentation (Mayes et al., 2010). Moreover, skin hydration also diminishes with age (Marrakchi & Maibach, 2007). All these suggesting that age was associated with skin hydration, although a previous study suggesting the contrary (Firooz et al., 2012).

Moreover, when comparing clinical skin characteristics by gender, significant distinctions were observed in the clinical parameters. A higher occurrence of spots that were UV-induced and brown in nature and higher levels of oil production were found in female compared to male. In contrary, the male group exhibited significantly higher sebum substance than the female, which can be related with the relative

plenitudes of *Staphylococcus* and *Corynebacterium* that utilize facial sebum as nutrients (Kim et al., 2013).

Kim et al (Kim et al., 2021) also found that the alpha-diversity index was essentially higher within the elderly, which was comparable to past reports that the older population had a better alpha differences than younger individuals for all skin microbiomes in Japanese women (Shibagaki et al., 2017). Differences in skin microbial differing qualities between men and women are likely emerges as a downstream impact of male and female steroid production (SanMiguel A, 2017).

The relative plentitude of skin microbiota between the younger and older groups affirmed that Actinobacteria and Proteobacteria, the two known major human skin phyla, are prevailing within the younger and older groups, separately. In fact, the sort of *Lawsonella* was more overwhelming and *Lawsonella clevelandensis* was recognized as a major species within the more younger group. *L. clevelandensis* was among the most common species on the human skin, scalp, and nostrils (Menezes et al., 2018). Furthermore, there was a critical negative relationship between *L. clevelandensis* and the cheek dampness substance and brown spots on the confront, in spite of the fact that the correlation was not strong (Menezes et al., 2018). Moreover, the *M. osloensis* is dominant in less-hydrated skin, which contrasts with the results of another study (Li et al., 2021).

A study was conducted on 73 Korean ladies living in urban population in Seoul. Study participants were divided into three age groups: (1) 10–29 years ($n = 24$), (2) 30–49 years ($n = 21$), and (3) 50–79 years ($n = 28$) (Kim, et al.). From the 73 subjects, 146 skin tests were collected (two skin locales per individual) by swabbing the brow metagenomic were sequenced on the Illumina MiSeq stage (Macrogen, Daejeon, Korea). Among all samples, 27 genera were reflected by $> 0.5\%$ of the total sequence average. *Pseudomonas* was the most prevalent and accounted for 17.8% of the overall arrangements on normal over all 73 hand tests, taken after by *Staphylococcus* (8.9%), *Acinetobacter* (7.4%), *Leuconostoc* (6.6%), *Weissella* (5.2%), *Streptococcus* (3.9%), *Bacillus* (3.5%), *Corynebacterium* (2.7%), *Cutibacterium* (2.5%), *Lactobacillus* (2.1%), *Enhydrobacter* (1.8%), *Rothia* (1.2%), *Aerococcus* (1.1%), *Stenotrophomonas* (1.1%), *Micrococcus* (1.0%), *Dietzia* (0.9%), *Erwinia* (0.9%), *Fingoldia* (0.7%), *Neisseria* (0.7%), *Xanthomonas* (0.7%), *Paracoccus* (0.7%), *Chryseobacterium* (0.6%), *Haemophilus* (0.6%), *Dermacoccus* (0.6%), *Actinomyces* (0.5%), *Anaerococcus* (0.5%), and *Methylobacterium* (0.5%). No taxon were different among the three age groups based on the LEfSe investigation. Among these 27 major genera, *Leuconostoc* expanded directly with increasing age ($p < 0.05$), while *Corynebacterium*, *Cutibacterium*, *Staphylococcus*, *Weissella*, and *Xanthomonas* diminished directly with increasing age ($p < 0.05$) (Kim, et al. 2019).

Alpha and Beta diversity investigations at slightest 36,710 sequences evenly on normal from all age categories were gotten after quality- and taxonomy-filtration methods. Diversity investigations was conducted by clear BIOM tables utilizing the most reduced sequencing depth to normalize the number of ASVs per test. Good's scope was $>99.2\%$ for all tests. All diversity qualities files in forehead skin expanded straightly with age, while no differences index increased or diminished straightly with age in hand skin (Kim, et al. 2019).

Skin microbiota has mutual relation that protect skin from attack by pathogens (Byrd et al., 2018), and microbiota composition may affect/change by age (Shibagaki et al., 2017). Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria are major phyla on both forehead and hand skin (Kim et al., 2019). The relative abundance of these four phyla may be affected by race/ethnicity. On forehead skin, Actinobacteria and Proteobacteria were the most excessive phyla among Japanese individuals (Kim et al., 2019), The plentitude of Firmicutes on skin of Korean individuals may be influenced

by dietary way of life related with dietary lifestyle especially Kimchi, that's broadly expended by Korean individuals. *Lactobacillus*, *Weissella*, and *Leuconostoc* placed inside Firmicutes are overwhelming genera that enormously contribute to Kimchi aging (Park et al., 2012). All these three genera were major taxa over all skin samples, whereas arrange *Lactobacillales* within Firmicutes counting uncultured lactic acid microscopic organisms was reflected by more than 13% of the total average sequences in collective data (Park et al., 2012). These taxa appear to contribute to the addition within the plenitude of Firmicutes. Proteobacteria on forehead skin was more copious in older than more younger individuals among other races/ethnicities, in Japanese and Western European individuals (Jugé et al., 2018). It has been detailed that commensal skin microbiota can prevent colonization of pathogens by regulating the expression of immune factors (Belkaid & Segre, 2014). Since Proteobacteria being pathogenic microbes, it decrease the ability of older to prevent the invasion of pathogens.

In any case, Proteobacteria remain difficult to understood because of rare cultured isolates (Cosseau et al., 2016). A previous study found that the alpha diversity of forehead skin were higher in older individuals than in the younger skin population (Leung et al., 2015). Higher alpha diversity from the forehead skin of older individuals have been detailed in both Japanese and Chinese population (Leung et al., 2015). This may be due to comparative ways of life and living situations in Asia. In any case, the alpha differing qualities taken of hand skin were not different among the older, showing that age-related changes in alpha differences are related to skin area.

Skin microbiome of Thai females

A study of skin microbiome was conducted on 30 Thai females with healthy skin. The subjects were divided into several groups: 10 teenage.heal (19–24 years), 10 teenage.acn (19–24 years), and 10 elderly.heal (51–57 years) (Somboonna et al., 2017). The teenage.heal represent to an age- and sex-matches to the teenage.acn, whereas a sex- and typical skin condition matches to the elderly.heal. To collecting these samples, all members not allowed to use took topical/ oral anti-microbials within the past 7 (topical) or 3 (oral) days. The subjects did not wash their faces for more than 8 h. For each person, a region of 1 × 1 inch of right and left cheeks, and 1 × 1 inch of forehead were swabbed. This study found that the bacterial orders and their relative plenitude reflected closer community relationship between teenage.acn and elderly.heal, taken after by teenage.acn and elderly.heal. Proteobacteria (48.73% teenage.heal, 45.08% teenage.acn, and 44.60% elderly.heal) and Bacteroidetes (8.36% teenage.heal, 13.60% teenage.acn, and 17.27% elderly.heal) were found among the three groups. Bacteroidetes and Firmicutes were more common in teenage.acn and elderly.heal than that of within the teenage.heal group (Somboonna et al., 2017).

The metabolic advantages of the microbial populace among the three centered groups uncovered a particular skin characteristics that can recognize these groups. For cases, the metagenomics-rapid annotation using subsystems technology (mg-RAST) subsystem of dormancy and sporulation, of spore DNA protection functional groups, were one of a kind to teenage.acn and elderly.heal. This characteristic may support both teenage.acn and elderly.heal commonly have lower skin moist/dry skin i.e., roughness and wrinkles. The basic lower moisture might initiate secretion of lipid in teenage.acn that can grow the certain bacteria (Somboonna et al., 2017).

Information comparison from diverse topographical areas, Thai versus U.S. females' skin microbiome, illustrated high diversity in their microbial profiles and functional possibilities (Costello et al., 2008). This supports the past study of variety in skin microbiome over ethnicities and geological areas (Costello et al., 2008). Bacterial diversity was indicated in extremophiles; Firmicutes and *Deinococcus-Thermus* were

commonly found among the Thai samples whereas Actinobacteria are more common among the U.S. tests (information not appeared). Hence, critical contrasts in up to 14 useful groups having a place to 9 metabolic subsystems (virulence, disease and defence; stress response; clustering-based subsystems; regulation and cell signalling; secondary metabolism; respiration; metabolism of metabolic compounds; membrane transport; and cofactors, vitamins, prosthetic groups, pigments) were be fathomed between the microbiome profiles from Thai and U.S.

Conclusion

Several studies have reported age-related changes in skin microbiome diversity. It has been reported that bacterial alpha diversity is higher in older adults. In aging individuals, there was a significant increase in *Corynebacterium* on the cheeks and forehead and *Acinetobacterium* on the scalp in the elderly group. In contrast, *Cutibacterium* was reduced on the cheeks, forehead, and forearms. Aging is also associated with increased abundance of Colibacterial taxa such as *C. cloppenedtin* and *C. amycolatum* in the forehead region.

Authors' contributions

Conceptualization: DR, WY and ZZ; Data curation: DR; Formal analysis: DR; Investigation: DR; Methodology: DR, WY and ZZ; Project administration: ZZ; Resources: DR, WY and ZZ; Supervision: DR, WY and ZZ; Validation DR, WY and ZZ; Writing-original draft preparation: DR, WY and ZZ; Writing-review and editing: DR, WY and ZZ.

Conflict of interest

There is no conflict of interest was reported by the authors.

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