

ORIGINAL RESEARCH

# Scalp Biophysical Characteristics in Males with Androgenetic Alopecia: A Comparative Study with Healthy Controls

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Division of Dermatology, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand **Background:** Androgenetic alopecia (AGA) is the most common type of hair loss in men. Its prevalence increases with advancing age. Characteristics of hair loss in male AGA reveal the possibility of different biophysical and physiological profiles between androgen-sensitive (vertex) and androgen-insensitive (occipital) scalps. However, these variations have not been well investigated.

**Objective:** We aimed to evaluate and compare scalp biophysical and physiological characteristics in male AGA patients and healthy controls.

**Methods:** Scalp biophysiological profiles were evaluated by non-invasive measuring techniques, including skin surface lipids (SSL), transepidermal water loss (TEWL), and stratum corneum hydration (SCH) on both vertex and occipital areas. Values were compared between scalp areas and study groups. Participants with AGA were further categorized based on disease severity (Hamilton–Norwood classification) for subgroup analyses. Correlation coefficients were evaluated to determine the effects of AGA severity and age on each functional parameter.

**Results:** Participants were 31 AGA subjects and 31 healthy controls. The vertex scalp of AGA patients had significantly higher SSL (p = 0.03) and lower SCH (p = 0.02) compared to the occipital scalp. TEWL was not significantly different (p = 0.31). AGA group SSL showed a positive correlation with severity of hair loss (r = 0.61, p = 0.03). When compared to controls, the AGA group vertex scalp had significantly higher SSL (p = 0.03) and lower TEWL (p < 0.001). The occipital area showed no statistically significant differences.

**Conclusion:** Male AGA presents with different biophysical and physiological characteristics in androgen-sensitive and androgen-insensitive areas, and with further differences from controls. These findings could direct further research and aid in the development of optimal hair and scalp treatments to improve scalp functional profiles in particular patients.

Keywords: alopecia, hair loss, hydration, sebum, transepidermal water loss

## Introduction

Androgenetic alopecia (AGA) is the most common type of hair loss, it affects up to 80% of males with genetic predisposition.<sup>1</sup> The prevalence of AGA increases steadily with advancing age.<sup>2</sup> It is characterized by a progressive miniaturization of hair follicles limited to the frontotemporal and vertex areas, considered to be androgen-sensitive scalp regions.<sup>3–5</sup> The pathogenesis of male AGA remains unclear; however, dihydrotestosterone (DHT), the main androgen converted from testosterone by 5-alpha reductase (5-AR), is thought to play an important role. DHT

Correspondence: Poonkiat Suchonwanit Division of Dermatology, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, 270 Rama VI Road, Ratchathewi, Bangkok, 10400, Thailand Tel +66-2-2011141 Fax +66-2-201-1211 ext 4 Email poonkiat@hotmail.com acts on androgen receptors (AR), causing terminal hairs to convert to miniaturized hairs, eventually resulting in AGA.<sup>2,6–9</sup>

The stratum corneum (SC) is a multilayered structure that acts as a barrier and regulates biological functions of the skin. Its specific biophysical and physiological properties vary between different body regions according to regional modifying factors. 10,11 Scalp skin features specific characteristics compared to skin of other body areas; it has high proportions of hair follicles, sebaceous glands, and blood vessels. 12 Increasingly, studies are finding that as well as hair follicles, androgen might also affect surrounding connective tissues and pilosebaceous units of balding scalp. Androgen-sensitive areas display significant enlargement of sebaceous glands, higher levels of DHT, and higher AR numbers compared to androgeninsensitive scalp areas. 13,14 Moreover, hair serves to protect the scalp from environmental stressors such as ultraviolet (UV) radiation, chemical agents, and trauma. 15 Therefore, scalps with alopecia have impaired physical defenses that might affect scalp biophysiological functioning. Several existing studies have already demonstrated abnormal barrier function in association with various skin conditions. We hypothesize that these factors might alter functional characteristics of AGA-affected scalps.

There is a paucity of information regarding biophysical and physiological profiles of scalp skin in AGA patients. One study has demonstrated that androgen-sensitive scalps have higher skin lipid levels and lower skin hydration compared to androgen-insensitive areas. However, to our knowledge, no comparative study with healthy controls has been conducted. The objective of this study was to evaluate and compare scalp skin barrier functions, including skin surface lipids (SSL), transepidermal water loss (TEWL), and SC hydration (SCH), in Thai males with AGA and healthy controls.

# **Materials and Methods**

This study was approved by the Mahidol University Institutional Review Board for Ethics in Human Research (MURA2019/308) and was performed in accordance with the Helsinki Declaration. Written informed consent was received from each subject before enrolment. The sample size was calculated based on data from a previous study comparing skin functional properties between androgen-sensitive and androgen-insensitive scalps. <sup>16</sup> A minimal sample size of 20 subjects per group

was required to achieve a power of 80% with a confidence level of 95%.

# **Participants**

A case-control study was conducted at the outpatient department, Division of Dermatology, Faculty Medicine, Ramathibodi Hospital from May December 2019. That males aged 18-70 years with a clinical diagnosis of AGA were recruited, and healthy subjects were enrolled as controls. Exclusion criteria included the presence of other hair and scalp disorders, and the use of topical/systemic drugs or systemic diseases that impaired skin barrier function and affect the hair growth cycle. Demographic data were collected from all subjects. Participants were instructed to avoid hair and scalp products 24 hours before examination.

## Measurements

All measurements were carried out by a well-trained and experienced investigator under standardized conditions at a controlled temperature of 19–24°C and relative humidity of 50%-58%. All subjects were in a climate-controlled room for at least 15 minutes before examination. Measurement of SSL, TEWL, and SCH were performed DermaLab<sup>®</sup> (Cortex Technology, Hadsund, Denmark) on two scalp areas for each subject. The hairs of the measured areas were trimmed at the level of the scalp surface immediately before the evaluation. Measurements were taken at the vertex (androgensensitive), located on the midline 24 cm from the frontal hairline, and the occipital region (androgen-insensitive), located on the midline 30 cm from the frontal hairline. Values were compared between scalp areas and study groups.

SSL was collected by placing microporous film on the scalp surface. The film's translucency was modified by the amount of sebum collected, changing the amount of light that could pass through and reach a reader module. TEWL was assessed via a probe using an open chamber method. The sensor detected the humidity, and the evaporation rate was recorded in units of g/h/m². SCH was measured by detecting any alteration of skin conduction properties when subjected to alternating voltage.

#### **Statistics**

Statistical analysis was performed using SPSS, version 18.0 (SPSS Inc., Chicago, IL, USA). Unpaired *t*-test and Mann–Whitney *U*-test were used to determine the differences

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between parameters in the AGA and control groups. Subgroup analyses based on disease severity were performed using the analysis of variance or the Kruskal–Wallis test. When the overall comparison p value was less than 0.05, pairwise comparisons of subgroups were conducted using the Turkey's honest significance difference test or the Mann–Whitney U-test as appropriate. Correlations between each variable and AGA severity, and age were determined using Spearman's and Pearson's correlations, respectively. Statistical significance was determined as p < 0.05.

# Results

# Characterization of the Participants

There were 31 males with AGA and 31 healthy controls in this study. Mean age for the AGA and control groups was  $51.25 \pm 10.19$  years and  $47.81 \pm 9.38$  years, respectively. Regarding Hamilton–Norwood classifications, 10 (32%) AGA cases were grade III, 8 (26%) were grade IV, 7 (23%) were grade V, 3 (9.5%) were grade VI, and 3 (9.5%) were grade VII. There was no statistically significant difference in demographics between the groups. Subject characteristics are summarized in Table 1.

# Scalp Biophysical Characteristics of Subjects with AGA

In the AGA group, the vertex had a statistically significant higher median SSL (8 [IQR 1–29] vs 3 [IQR 1–10], p=0.03) and lower mean SCH (87.84  $\pm$  18.75 vs 102.96  $\pm$ 

Table I Characteristics of Included Participants

	AGA N = 31	Control N = 31	p value
Age, y Mean (SD)	51.25 (10.19)	47.81 (9.38)	0.17
Hamilton-Norwood type, n (%) III IV V VI VII	10 (32) 8 (26) 7 (23) 3 (9.5) 3 (9.5)	- - -	-
Frequency of hair washing,  n (%)  < I time/day  I time/day  ≥ I time/day	8 (25.8) 21 (67.7) 2 (6.5)	14 (45.1) 15 (48.4) 2 (6.5)	0.76

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

29.29, p=0.02) as compared to the occipital area. However, the vertex showed slightly lower mean TEWL compared to the occipital scalp, although this was not statistically significant (16.3  $\pm$  5.15 vs 18.1  $\pm$  4.2, p=0.31) (Figure 1).

# Subgroup Analyses of Subjects with AGA

Participants with AGA were further categorized based on disease severity (Hamilton–Norwood classification). The overall comparisons among AGA subgroups and pairwise comparisons between each severity subgroup revealed no statistically significant differences in any of the measured values. Almost all parameters including TEWL, SCH, and occipital SSL revealed weak correlations with AGA severity. However, only vertex SSL showed a statistically significant positive correlation with AGA severity (r = 0.61, p = 0.03) (Figure 2). No correlation was found between the parameters and increasing age in both groups (all r < 0.1).

# Comparisons of Scalp Biophysical Characteristics Between AGA and Control Groups

Comparing measured values between AGA and control groups, median SSL on both vertex and occipital areas in the AGA group was higher compared to controls, but only vertex SSL was significantly different (p = 0.03). In contrast, mean TEWL was lower in the AGA group than in controls for both the vertex and occipital areas, with the vertex presenting a highly significant difference (p < 0.001). Mean SCH was lower in the AGA group than in controls for both areas; notably, mean vertex SCH tended to be lower than occipital SCH for both groups (Table 2).

## **Discussion**

Our study revealed differences in biophysiological characteristics between androgen-sensitive and androgen-insensitive scalp areas of individuals with AGA. The vertex had significantly higher SSL and lower SCH compared to the occipital scalp. Our results are consistent with a previous study, which also reported higher SSL and lower SCH for androgen-sensitive vs androgen-insensitive scalps. Furthermore, our study is the first to compare the scalp profiles of AGA patients and healthy controls. We demonstrated significant differences between the two groups in terms of higher vertex SSL and lower vertex TEWL in AGA patients, but comparable occipital

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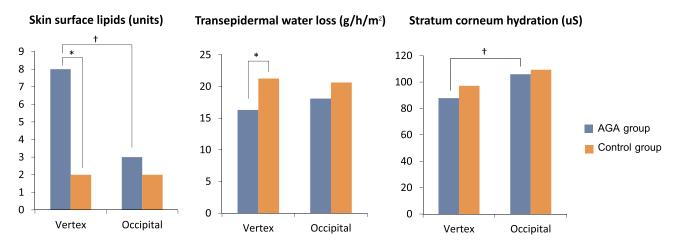


Figure I Values of skin surface lipids, transepidermal water loss, and stratum corneum hydration measured at vertex and occipital areas of males with androgenetic alopecia (AGA) and healthy controls. †Statistically significant difference between vertex and occipital areas of males with AGA, \*Statistically significant difference between AGA and control groups.

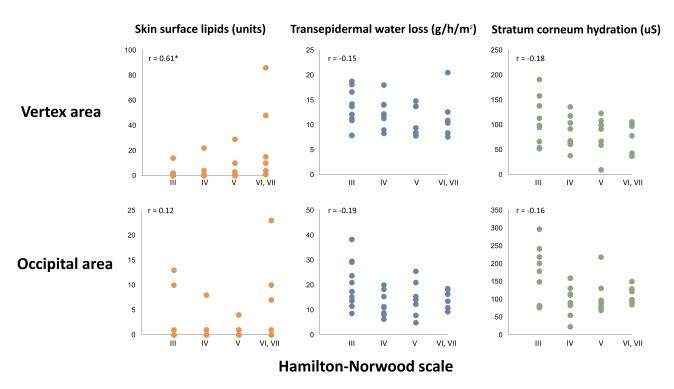


Figure 2 Scatter plots of skin surface lipids, transepidermal water loss, and stratum corneum hydration measured at vertex and occipital areas of males with androgenetic alopecia, showing correlation coefficient (r). \*Statistically significant.

area values. Our findings indicate alterations of skin barrier function in the scalps of AGA patients.

SSL comprises lipid components that originate in the epidermal lamellar bodies and sebaceous glands. <sup>17,18</sup> It evenly overlays SC surface, providing specialized protective functions and regulating permeability barrier homeostasis. <sup>17,19</sup> Our study demonstrated several SSL alterations on AGA-affected scalps: (1) significantly higher vertex SSL as compared to occipital SSL on AGA

scalps; (2) positive correlation of SSL with AGA severity; and (3) significantly higher vertex SSL for the AGA group as compared to controls. We postulate that the role of androgens in AGA pathogenesis could explain our findings. Sawaya et al reported greater 5-AR enzymatic activity increasing conversion of androgens to DHT at AGA-affected areas.<sup>20</sup> Moreover, sebaceous glands on balding scalps reveal higher binding affinity for DHT and express significantly higher ARs than healthy scalps.<sup>13,14</sup> Apart

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Table 2 Comparison of Measured Values Between Androgenetic Alopecia and Control Groups

Biophysical Parameter	AGA N = 31	Control N = 31	p value
Skin surface lipids, median (IQR)			
Vertex area	8 (1–29)	2 (1–9)	0.03*
Occipital area	3 (1-10)	2 (1–8)	0.32
Transepidermal water loss, mean (SD)			
Vertex area	16.35 (5.15)	21.26 (6.26)	<0.001*
Occipital area	18.14 (4.20)	20.64 (5.98)	0.93
Stratum corneum hydration, mean (SD)			
Vertex area	87.84 (18.75)	97.17 (20.8)	0.07
Occipital area	105.96 (29.29)	109.32 (31.01)	0.41

Note: \*Statistically significant.

Abbreviations: AGA, androgenetic alopecia; IQR, interquartile range; SD, standard deviation.

from promoting follicular miniaturization, DHT also upregulates sebocyte differentiation, leading to increased size of sebaceous glands in AGA-affected scalps.<sup>21</sup> Kim et al confirmed these effects by demonstrating significant sebaceous gland enlargement and decreased hair follicle size in frontal and vertex areas compared to occipital scalp using serial cross-sectional histology and threedimensional reconstruction software.<sup>22</sup> Sebum production was found to be under hormonal control, and it increases with androgen activity. 12 Therefore, AGA-affected areas show increased DHT activity and larger sebaceous glands producing more sebum, possibly resulting increased SSL.

TEWL refers to the amount of water evaporating through the epidermis due to the water vapor pressure gradient across the skin. It varies across different body areas and can be affected by multiple factors. SC thickness influences skin TEWL and may explain our finding of lower vertex TEWL in AGA patients. Ya-Xian et al reported a negative correlation between number of corneocyte layers and TEWL, indicating that water barrier function of the skin related to SC thickness. 10 Czekalla et al demonstrated the effect of UV radiation by showing that sun-exposed skin has a thicker epidermis and SC than sunprotected areas.<sup>23</sup> In our study, AGA subjects showed lower vertex TEWL than occipital TEWL. Further, we found significantly lower vertex TEWL for AGA patients as compared with controls. Vertex scalp is more commonly exposed to UV than the occipital area due to perpendicularity of the scalp surface to light. In addition, AGA patients have reduced hair in this area. We theorize that vertex scalps with high UV exposure could result in thickening and eventually decreased TEWL.

Furthermore, reduction of hair density and diameter on AGA-affected scalps may diminish TEWL since a metaanalysis reported a trend to decrease TEWL among body areas with a lower number of hair follicles.<sup>24</sup>

The quantity of water contained in SC, or SCH, is crucial for maintaining normal biophysiological functioning of the epidermis. Skin water content is altered by several factors, including an individual's volume status, microcirculation, UV exposure, surrounding temperature, and humidity.<sup>25</sup> Our study revealed significantly lower vertex compared to occipital SCH in AGA patients, but no significant difference in SCH between AGA and control groups. Scalp surface occlusion and UV exposure could explain our results. Kleesz et al reported that skin occlusion increased SCH approximately 30%, while SC thickening decreased SCH 10-20%. 11 Compared to the occipital area, balding scalps have reduced hair coverage providing relatively less occlusive effects. As a result, there is more UV exposure and consequent increased SC thickness.<sup>23</sup> This leads to significantly lower vertex as compared to occipital SCH in AGA patients. In the control group, SCH values echoed the AGA group, with vertex SCH lower than that of the occipital scalp, although this was not statistically significant. These findings may indicate scalp protective properties of hair fibers from the environment.

Evidence suggests that altering the biophysiological profiles of AGA-affected scalps impacts disease severity. Lai et al reported that AGA patients frequently presented with oily scalps, and this was associated with moderate to severe AGA.<sup>26</sup> Their findings correspond with ours: increased vertex SSL in the AGA group, and a positive correlation between SSL and AGA severity. In addition to genetic susceptibility and androgen involvement, scalp

microinflammation might also contribute to AGA pathogenesis, accelerating disease onset and increasing its severity. <sup>27–31</sup> Gatherwright et al conducted a study of 92 male identical twins who developed AGA to different stages; the presence of inflammatory scalp correlated with more severe AGA. <sup>32</sup> Skin with low SCH exhibits increased levels of local and systemic pro-inflammatory cytokines. <sup>33–35</sup> In contrast, SCH improvement appears to reduce these inflammatory substances. <sup>36</sup> Therefore, prescribing optimal hair and scalp products that reduce SSL and enhance SCH alongside standard medical treatment could improve treatment outcomes.

The limitations of this study include the relatively small number of subjects, homogenous population (Asians), and the single center nature, as such, the results might not represent the general population. A multicenter study conducted with a larger subject group in different ethnicities would minimize these limitations. For more precise results, participants should be instructed to use the same shampoo/scalp cleanser for 1-2 weeks, with the last shampoo performed 24 hours before the measurement. Besides, variables such as occupations, UV exposure, diet, and daily activities should be collected since they may affect individuals' scalp biophysical properties. Assessing skin thickness using scalp histopathology and/or ultrasonography could help better understanding scalp biophysical alterations. In addition, further research is required to elucidate whether biophysical parameters, especially SSL, are associated with AGA severity.

# **Conclusion**

This study furthers our understanding of the biophysical and physiological characteristics of AGA-affected scalps and how they differ from non-AGA-affected scalps. The information reported herein could provide important reference values for further research of AGA in Asian populations. Moreover, our findings could guide development of optimal hair and scalp care products to improve treatment outcomes in patients.

# **Data Sharing Statement**

All datasets are available from the corresponding author on reasonable request.

# Ethics Approval and Consent to Participate

This study was approved by the Mahidol University Institutional Review Board for Ethics in Human Research (MURA2019/308) and was performed in

accordance with the Helsinki Declaration. Written informed consent was received from each subject before enrolment.

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# **Disclosure**

The authors report no conflicts of interest in this work.

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