clinical, laboratory and trichoscopic features of pediatric androgenetic alopecia: a retrospective analysis in 133 patients

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Abstract

This retrospective study from Jiangsu Province Hospital elucidates the prevalence and impact of pediatric androgenetic alopecia (AGA). Over a period of 14 years, 133 patients under the age of 18 were studied, with manifestations appearing as early as 8 years of age. Of note, 39.8% had an overweight/obese and 78.2% reported a family history of AGA. Comorbidities included seborrhoeic dermatitis (51.9%), acne (42.9%) and sleep disorders (28.6%). In addition, 4.5% had polycystic ovarian syndrome. Hormonal imbalances such as low sex hormone-binding globulin (47.1%) and vitamin D deficiency (61%) were common, as was low ferritin (23.6%). Male AGA patterns were characterised by crown thinning and temporal variations, whereas females showed crown thinning with frontal hair retention. Trichoscopic differences were observed between genders and age groups. This study highlights the importance of individualised, stepwise and comprehensive treatment, prioritising hormonal disorders and comorbidities when treating hair loss with topical minoxidil. Encouraging patients to adhere to regular medication and follow-up appointments can lead to favourable outcomes.

Introduction

Androgenetic alopecia (AGA) is the most common type of hair loss after adolescence, with a high prevalence of 21.3% among males and 6.0% among females in China[1]. AGA presents as diffuse hair loss in the frontal and temporal areas in men, in women it is characterized by thinning of hair on the top of the head, widening of the part, and less recession of the frontal line. Although the specific pathogenesis of AGA is still unclear, it is believed to be mainly related to genetics and androgen levels. Eventhough AGA is not considered as a life-threatening medical condition, it can significantly impact patients' self-esteen and qulity of life.

The prevalence of pediatric androgenetic alopecia has been on a steadily rise over the past few decades, which is widely recognized to have correlation with hyperinsulinemic diet and higher levels of circulating androgen exposure at a younger age, resulting in early onset in genetically susceptible children[2,3]. In addition, studies have shown that early-onset AGA is associated with metabolic syndrome[4-6], which includes conditions such as overweight, insulin resistance, hyperglycemia, and dyslipidemia[7,8]. Furthermore, polycystic ovary syndrome (PCOS) is also frequently present among female patients[9,10].

Researches available about early-onset AGA in pediatric patients is currently limited, with most studies have a relatively small sample size to generalize study findings. Additionally, data on Chinese pediatric AGA has not yet been published. Therefore, the objective of this retrospective study is to analyze the clinical features, family history, BMI, comorbidities, laboratory test results, and trichoscopic features of 133 AGA pediatric patients visited the hair disease clinic of the Dermatology Department at Jiangsu Province Hospital in China from 2010 to 2023.

2 Methods

2.1 Study patients

Pediatric patients with early-onset AGA who were registered at the hair disease clinic of the Dermatology Department in Jiangsu Province Hospital, China, between 2010and 2023 were selected. Patients under age of 18

with a definitive diagnosis of AGA were selected for data collection and analysis.and any uncertain information was confirmed through telephone follow-up.

2.2 Collection of Demographics and Laboratory Tests

Patient demographics and medical history information were collected from medical records, including age, gender, age at disease onset, and duration of AGA.Height and weight were also collected to calculate patients' body mass index (BMI). Laboratory test results including sex hormone-binding globulin (SHBG), vitamin D (Vit-D), testosterone, ferritin, and total prostate-specific antigen (TPSA).

2.3 Analysis of Comorbidities

China established specific classification standards as follows: overweight (BMI 24-27.9 kg/m2) and obesity (BMI ≥ 28 kg/m2). During outpatient consultations, a comprehensive medical history was obtained from each patient, including existing conditions of Polycystic Ovary Syndrome (PCOS), acne, seborrheic dermatitis, hirsutism, and sleeping disorders.During routine outpatient assessment, experienced physicians diagnose if patient has seborrheic dermatitis and document presented symptoms to confirm the diagnosis.

2.4 Hair Loss Classification and Trichoscopy

Hair distribution pattern for males follows the BASP classification, while females utilize the Ludwig classification[11,12]. Trichoscopy was utilized with high-resolution imaging systems and advanced software for image analysis, enabling precise assessment of hair in different scalp regions. Parameters such as hair density, hair diameter, percentage of terminal hair, and percentage of vellus hair were recorded to monitor changes in hair growth for the patients.

2.5 Statistical Analysis

Data were presented as mean ± SD or n of patients (%). Categorical data were analyzed by using the chi-square test. P-value < 0.05 was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics 26 software.

Reviewed and approved by the Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University.All methods were performed in accordance with the relevant guidelines and regulations.

3 Results

3.1 Patient Characteristics and Hair Loss Patterns

A sample of 133 pediatric patients were selected, including 60 males and 73 females,diagnosed with AGA at Dermatology department of JiangSu Province Hospital between 2010 and 2023. The mean age of the patients was 15.5 years (range: 10-17). Females had a slightly lower mean age than males (15.05 vs. 16.19 years, respectively) and a lower mean age at disease onset (13.41 vs 14.44 years, respectively) in different age groups. The onset of AGA symptoms before they first seek medical care ranged from 4 months to 3 years, with a mean duration of 1.72 years. There was no significant difference in course of disease between males and females (male: 1.76 years, female: 1.70 years). The patient characteristics are summarized in Table 1.

Table1 Age at presentation,onset and duration of AGA in pediatric.

Age	Age at presentation years(mean±SD)	Age at onset,years(mean±SD)	Duration,years(mean±SD)
≤17years	15.6±1.7	13.9±2.0	1.7±1.3
Males(n=43)	16.2±1.1	14.4±1.9	1.8±1.4
Females(n=56)	15.1±1.9	13.4±2.0	1.7±1.3
10-14years	12.9±1.2	11.8±1.9	1.3±1.1
Males(n=4)	13.5±1	12±2.3	1.8±1.7
Females(n=18)	12.7±1.2	11.8±1.9	1.1±0.9
>14-17years	16.3±0.7	14.4±1.6	2.0±2.0
Males(n=39)	16.5±0.7	14.7±1.7	1.8±1.4
Females(n=38)	15.8±2.5	14.2±1.5	2.3±2.4

Abbreviations: SD, standard deviation;AGA:androgentic alopecia

Pediatric patients with AGA exhibited a hair loss pattern similar to What we've seen in adults. Male pediatric patients experienced diffuse thinning in the crown and varying degrees of temporal thinning, while female pediatric patients typically experienced diffuse thinning in the crown with a preserved frontal hairline. However, 5 male patients present with Christmas tree-like pattern of hair loss with a preserved hairline and a thinning crown (Figure 1 and 2).

Among our study sample, 39.8% were identified as overweight or obese. It came to our attention that the prevalence of overweight and obesity was notably higher among patients aged 14-17 years compared to those aged ≤14 years (33.3% vs. 6.3%). Detailed distribution of overweight and obese participants in our study is outlined in Table 2.

Table 2. BMI and concomitant disease of the different age groups [n(%)]

	>14-17	≤14	Total
Overweight (BMI 24-27.9kg/m^2)	24（21.4%）	3（2.7%）	20（24.1%）
obesity (BMI ≥ 28 kg/m^2)	8（7.1%）	1（0.9%）	24（8.0%）
acne	53（39.8%）	4（3.0%）	57（42.9%）
Seborrheic dermatitis	53（39.8%）	16（12.0%）	69（51.9%）
Hairy and bearded	37（27.8%）	7（5.1%）	44（33.1%）
PCOS	5（3.8%）	1（0.8%）	6（4.5%）
Difficulty sleeping	33（24.8%）	5（3.8%）	38（28.6%）

Abbreviations:BMI: Body Mass Index;PCOS: polycystic ovary syndrome;

Seborrheic dermatitis was identified as the most prevalent comorbidity associated with pediatric AGA, with a leading prevalence rate of 51.9% (69 of 133), followed by acne with a prevalence of 42.9% (57 of 133). Followed by rates of hirsutism (33.1%) and sleep disturbances/insomnia (28.6%). Remarkably, the prevalence of these comorbidities varied significantly among different age groups, with a higher incidence observed among patients aged >14-17 years as compared to those aged ≤14 years.

3.3 Pediatric AGA family history

Our study results indicate that the majority of pediatric patients with early-onset AGA had a family history, with 78.2% (104 out of 133). Among the male and female patients, 81.7% and 75.3%, respectively, had a positive family history. Further analysis showed that 43.3% of male patients and 21.9% of female patients reported father with AGA, while 16.7% of male patients and 35.6% of female patients mothers. Both parents were affected in 21.7% of male patients and 17.8% of female patients.

3.4 Related laboratory test of pediatric AGA patients

Table 3 presents the results of laboratory results for low SHBG, Vitamin D deficiency, high testosterone, and low ferritin levels in the study sample. Among the study participants, 10 females exhibited increased levels of both free and total testosterone level. Low SHBG was observed in 56 of 119 pediatric patients (47.1%), with a slightly higher proportion in males (48.2%) than females (46.0%). Vitamin D deficiency was prevalent in 61% of the study population, with a significantly higher incidence rate in females (71.4%) compare to males (49.1%). Moreover, 26 of 110 pediatric patients had low ferritin levels(23.6 %), with a higher incidence rate in females (33.9%) compared to males (10.4%).

Table 3 Related laboratory test in Pediatric of AGA

test	Male(n=56)	Female(n=63)	Total
Low SHBG	27(48.2%)	29(46.0%)	56(47.1%)
Vit-D deficiency	27(49.1%)	45(71.4%)	72(61.0%)
High Testosterone	0	10(16.1%)	10(16.1%)
Low Ferritin	5(10.4%)	21(33.9%)	26(23.6%)

Abbreviations:SHBG: sex hormone-binding globulin;Vit-D: vitamin D;

3.5 Female patients with PCOS.

In our study, 6 female patients with AGA were also diagnosed with polycystic ovarian syndrome (PCOS) prior to their referral to Jiangsu Provice Hospital. Information regarding their age of treatment, hair loss grade, comorbidities, and laboratory test results is provided in Table 4.

Table 4 Six girls clincial and laboratory test with androgentic alopicia and PCOS.

Patient	Age(year)	Ludwing grading	BMI	Acne	Seb	SHBG	Vit-D	Testo	Ferritin
1	17	I	27.22	-	-	↓	↓	Nor	Nor
2	17	I	20.82	_	+	Nor	Nor	Nor	Nor
3	16	II	19.53	-	-	↓	↓	↑	↓
4	16	I	22.03	+	+	↓	↓	Nor	Nor
5	16	I	21.26	+	+	Nor	↓	Nor	Nor
6	13	II	24.8	+	+	↓	↓	Nor	Nor

Abbreviations:SHBG: sex hormone-binding globulin;Vit-D:vitamin D;Seb: Seborrhoeic dermatitis;Nor:normal;PCOS: polycystic ovary syndrome;

3.6 The degree of hair loss at first visit

In male adolescent patients with pediatric AGA, the majority were classified as M type in the BASP classification. Specifically, the main hair loss level in males was concentrated in M1-M2 (80.4%), while specific type F was mainly distributed in F1-F2 (82.1%), and specific type V was mainly distributed in V1-V2 (80.4%). On the other hand, female patients were mainly (87.3 %) classified as type I-II in the Ludwig classification.

3.7 Clinical features of trichoscopy exams at first visit

We presents the trichosopic findings of our study regarding hair characteristics, including hair density, hair diameter, terminal hair ratio, and vellus hair ratio, among male and female pediatric participants stratified by age groups of ≤14 years old and >14-17 years old. In males, those aged 14 years or younger had a lower average hair density than those aged 14 to 17, but thicker hair diameter than younger children . Conversely, males aged 14 or above showed greater awareness and more likely to seek treatment of terminal hair than those under 14 years old. Among females, those aged 14 to 17 years old had higher hair density, hair diameter, and terminal hair ratio than those under 14 years old.[Table 5] Hair trichoscopic characteristics among pediatric AGA patients has similar features to adult androgenetic alopecia.[Figure 3]

Table 5. Clinical features of trichoscopy in first visit in Pediatric.

	Hair density(hairs/cm²)	Hair diameter(mm)	Final gross ratio(%)	Vellus Hair ratio(%)
Male (n=56)	155.86±34.78	0.06±0.01	76%±12%	24±12%
≤14 (n=7)	160.48±33.33	0.06±0.01	75%±9%	25%±9%
14-17 (n=49)	151.02±37.56	0.07±0.01	77%±13%	23%±13%
Female (n=63)	155.42±30.12	0.07±0.01	79%±12%	21%±12%
≤14 (n=18)	147.34±21.07	0.06±0.01	75%±12%	25%±12%
14-17 (n=45)	158.69±32.34	0.07±0.01	81%±11%	19%±11%

Discussion

In our study, the youngest AGA patient was 8 years old, which is slightly later than the previously reported earliest onset at 6 years old [13]. Females showed a higher incidence of AGA compared to males, which is consistent with some previous studies [13,14], but contradicts the findings of studies conducted by Gonzalez ME and Kim BJ [15, 16]. We speculate that the differences in AGA incidence could be attributed to the diverse genetic background and racial disparities between the populations included in Gonzalez's study, primarily Caucasians from Europe and America, and our study, mainly consisting of East Asian individuals. Furthermore, variations in lifestyle and environment between Europe-America and Asia, such as dietary habits, life stress, and environmental pollution, might contribute to the differing gender-specific incidence rates. Additionally, our study revealed that female patients tend to experience AGA at a younger age than male patients, as indicated by an earlier age of onset and initial visit. These findings align with other studies that have reported a slightly younger age of onset in female patients [13, 15, 16]. The significance lies in both patients and physicians increasing their awareness of the early onset of androgenetic alopecia, allowing for early detection, diagnosis, and treatment.

Furthermore, our study unveiled a higher prevalence of a family history of AGA in Chinese pediatric patients compared to that reported in other studies, with 78.2% of patients having a positive family history [13-16]. Paternal family history was more commonly observed than maternal history, with 81.7% and 75.3% of patients reporting respective family histories. Moreover, 19.5% of patients had a positive family history in both parents. Therefore, it is essential to raise awareness among pediatric patients with a positive family history, as they may experience hair loss at an earlier age.

Patients with AGA commonly present with concurrent skin conditions, most notably seborrheic dermatitis,acne and hirsutism. Therefore, it is important to monitor these associated diseases and adopt appropriate treatments. Especially for conditions such as seborrheic dermatitis, treatment for seborrheic dermatitis may contribute to improving hair loss to some extent. Moreover, it is worth mentioning that a considerable number of adolescent patients reported experiencing sleeping difficulties. It is well known that sleep deprivation/disturbance can lead to hormonal abnormalities, which is also a risk factor of AGA.Therefore, further study is needed to further investigate the effectiveness of treating sleep disturbance can reduce onset/ progression of pediatric AGA. It came to our attention that a previous retrospective study reported a PCOS prevalence of 47.4% in adolescent female with AGA, our study observed a much lower incidence of 4.5%. This discrepancy may be attributed to the fact that our study did not mendate diagnostic imaging to diagnose all female participants for PCOS, which potentially leads to the exclusion of some undiagnosed PCOS patients from data analysis.

In our study, Moderate hair loss was present in a significant proportion of patients at their first visit, and there were differences in hair density and diameter among different age groups, with female patients having significantly finer hair than male patients. Therefore, it is necessary to raise awareness of and perform early diagnosis and treatment for AGA in paediatric.

In the laboratory evaluations of pediatric AGA patients, we observed a notable proportion with low levels of vitamin D, sex hormone-binding globulin (SHBG), and ferritin. Notably, female patients were more susceptible to low vitamin D levels compared to males. The screening of these indicators, particularly in female patients, could aid in the diagnosis and treatment of pediatric AGA. Surprisingly, testosterone levels did not significantly influence height or show significant increases in male AGA patients. Furthermore, only a small percentage of female patients exhibited elevated testosterone levels, indicating that androgens may not play a dominant role in the pathogenesis of male pediatric AGA, and other factors and mechanisms may be involved.

AGA is extensively studied in adults, but there is limited knowledge about its occurrence and characteristics in younger individuals. This study represents one of the few investigations into AGA in children and adolescents and is the largest to explore the clinical features, laboratory test,trichoscopic characteristics, associated diseases, and laboratory results of AGA in the Chinese population. Our findings offer valuable insights into early clinical characteristics of pediatric AGA in this specific demographic population, shed some lights on future research directions and clinical practice guidelines in treating pediatric AGA patients.

Given the fact that our study is a retrospective study with a relatively small sample size from a single clinic site, the generalizability of our reseach findins may be limited. In addition, our study dose not have frequent routine testing for metabolic and hormonal indicators to analyze further correlations between hormonal changes with severity of pediatric AGA. Future researches with prospective multicenter designs and larger sample sizes are needed to increase representiveness and generalizability. and comprehensive testing to validate and extend our

findings. Furthermore, the psychological impact among pediatric AGA patients warrants further investigation on early intervention to reduce psychological stress among pediatric AGA patients.

Besides enhancing the understanding of androgenetic alopecia in children among dermatologists and pediatricians, there is a need for individualized, step-by-step, and comprehensive treatment. Initially, issues associated with hormonal disorders like seborrheic dermatitis, folliculitis, polycystic ovary syndrome, and acne are addressed. Subsequently, while addressing hair loss primarily with topical minoxidil, concurrent conditions such as vitamin D deficiency and iron deficiency are also managed. Encouraging patients to adhere to regular medication and follow-up appointments can often yield favorable outcomes.

Declarations

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Conflicts of Interest: None declared.

IRB approval status: Reviewed and approved by the Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University(Approval Number:2023-SR-354) .

Informed consent: Written informed consent have been provided by the patients and their legal guardians. They have also consented to the publication of their case details.

Author Contribution

CP L: Conceptualization, Methodology, Software, Investigation, Formal Analysis, Writing - Original Draft YG F: Data Curation, rewriting,supervision;YM D: Investigation,prepared figures 1-2;LB B: Resources, prepared figures 3;CF W: date collection and analysis;M Z: Modify tables and Review YB D: Investigation and resources;WX F (Corresponding Author):Conceptualization, Funding Acquisition, Resources, Supervision, Writing - Review & Editing.. All authors reviewed the manuscript.

References

1. Jiang W, Yan Q, Tu P, et al. Chinese expert consensus on diagnosis and management of androgenic alopecia in both males and females. *Int J Dermatol Venereol*. 2019;3(3):195-202.
2. Griggs Jacob,Burroway Brandon,Tosti Antonella.Pediatric androgenetic alopecia A review.*J Am Acad Dermatol*.2021;85[5]:1267-1273.
3. Alfredo R,Andrea D,Flavia P. The diagnosis of androgenetic alopecia in children: Considerations of pathophysiological plausibility.*Australas J Dermatol.*2019;60(4):279-283.
4. Sarkar P, Chakraborti K, Mondal S. Association of metabolic syndrome with early-onset androgenetic alopecia: a case-control study.*Iran J Dermatology.*2022;25(2):106-110.

5. Qiu Y, Zhou X, Fu S. Systematic review and meta-analysis of the association between metabolic syndrome and androgenetic alopecia[J].*Acta Dermato-Venereologica*.2022;102:645.
6. Memon FH, Rahimoon AG.Androgenetic alopecia as a marker of metabolic syndrome.*J Pharm Res Int*. 2021;33:146–153.
7. odríguez-Gutiérrez R,Salcido-Montenegro A,González-González JG.Early Clinical Expressions of Insulin Resistance:The Real Enemy to Look For.*Diabetes Ther.*2018;9(1):435-438.
8. Wang Y X,Chen X W,Wang S B,et al.Association between androgenic alopecia and coronary artery disease: a cross-sectional study of Han Chinese male population[J].*Int J Gen Med.* 2021;14:4809-4818.
9. Tu YA,Lin SJ,Chen PL,Chou CH,Huang CC,Ho HN,Chen MJ. HSD3B1 gene polymorphism and female pattern hair loss in women with polycystic ovary syndrome.J Formos Med Assoc.2019;118(8):1225-1231.
10. Sanke S, Chander R, Jain A, Garg T, Yadav P.A Comparison of the Hormonal Profile of Early Androgenetic Alopecia in Men With the Phenotypic Equivalent of Polycystic Ovarian Syndrome in Women.*JAMA Dermatol*.2016;152(9):986–991.
11. Lee WS, Ro BI, Hong SP. A new classification of pattern hair loss that is universal for men and women: basic and specific (BASP) classification. J Am Acad Dermatol.2007;57(5): 37-46.
12. Ludwig, E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex.*Br J Dermatol*.1977;97(3), 247-254.
13. Tosti A, Iorizzo M, Piraccini BM. Androgenetic alopecia in children:report of 20 cases.*Br J Dermatol*. 2005;152(3):556-559.
14. Özcan D.Pediatric androgenetic alopecia: a retrospective review ofclinical characteristics, hormonal assays and metabolic syndrome riskfactors in 23 patients.*An Bras Dermatol*. 2022;97(2):166-172.4.
15. Gonzalez ME, Cantatore-Francis J, Orlow SJ. Androgenetic alopecia inthe paediatric population:a retrospective review of 57 patients.*Br JDermatol*. 2010;163(2):378-385
16. Kim BJ, Kim JY, Eun HC. Androgenetic alopecia in adolescents: A report of 43 cases.*JDermatol*.2006;33(10):696-699

Figures

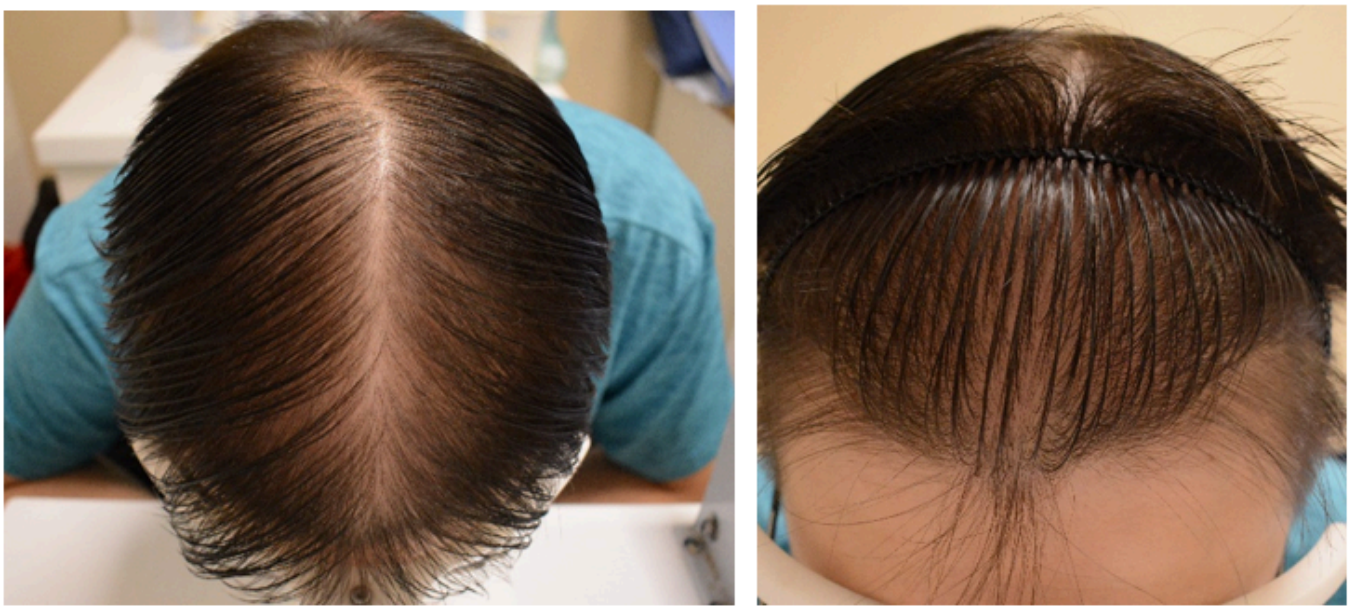

Figure 1

Hair loss patterns of a 15 years old male pediatric androgenetic alopecia.(A) “Christmas tree pattern”, experiencing diffuse thinning in the crown (B) preserved frontal hairline

Figure 2

Hair loss patterns of a 17 years old female pediatric androgenetic alopecia.(A and B) Female typically experience diffuse thinning in the crown with a preserved frontal hairline

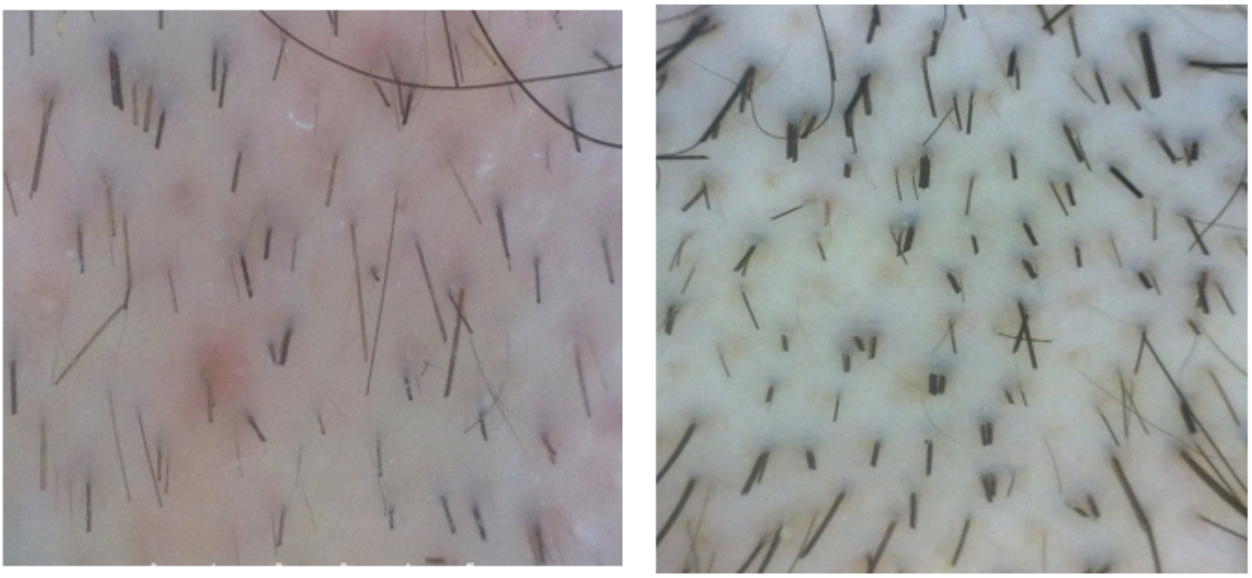

Figure 3

Trichoscopic findings of pediatric androgenetic alopecia. (Figure A is from male,Figure B is from female) The hair density is significantly reduced, hair diameter is diversity and the density of vellus is increased.