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Early-onset androgenetic alopecia in China: a descriptive study of a large outpatient cohort

Qi Ding[1,2,*], Yu-Xuan Xu[1,*], Wei-Ling Sun[1], Jing-Jing Liu[1], Yu-Yu Deng[1], Qiao-Fang Wu[1], Chun-Yu Cao[1], Lan-Bo Zhou[1], Yan Lu[1] and Wei-Xin Fan[1]

Abstract

Objective: To describe the clinical features of early-onset androgenetic alopecia (AGA) in a large cohort of Chinese patients.

Methods: This descriptive study recruited consecutive patients seeking medical treatment for AGA between 1 January 2013 and 30 November 2018. Patients were included in the study if they reported being ≤35 years old at AGA onset and if their pattern of hair loss was documented with photographs. The age of onset, sex, body mass index (BMI), BAsic and SPecific classification of hair loss and family history of alopecia were collected in an electronic database.

Results: A total of 3897 patients with early-onset AGA were recruited to the study. The majority of patients (70.6%; 2751 of 3897) were 21–30 years old and male (72.7%; 2834 of 3897). No association was found between high BMI (≥25 kg/m^2) and early-onset AGA. There were significantly more overweight male AGA patients than overweight female patients (86.8% [632 of 728] versus 13.2% [96 of 728], respectively). The overall prevalence of familial AGA was 72.8% (2837 of 3897) and the condition was inherited more often from the father (52.8%; 1498 of 2837) than from the mother (24.3%; 688 of 2837).

Conclusions: Early-onset AGA primarily affects male patients between 21–30 years of age. Males with early-onset AGA are likely to have inherited AGA from their fathers.

[1]Department of Dermatology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China
[2]Department of Dermatology, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province, China

*These authors contributed equally to this study.

Corresponding author:
Wei-Xin Fan, Department of Dermatology, The First Affiliated Hospital of Nanjing Medical University, 300 Guangzhou Street, Nanjing 210029, Jiangsu Province, China.
Email: hairman2019@163.com

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Introduction

Androgenetic alopecia (AGA) is the most common type of hair loss affecting both men and women.[1] It is characterized by the gradual replacement of terminal hairs in the central part of the scalp with short, thin, light hairs (vellus). In men, AGA is accompanied by bitemporal recession of the frontal hairline, followed by diffuse thinning at the vertex. In women, AGA causes diffuse thinning in the crown region but the frontal hairline is often retained, a pattern known as the Ludwig pattern.[2] The incidence and prevalence of AGA vary with age and ethnicity. For example, AGA affects approximately 50–70% of Caucasian men and 40% of Caucasian women by the age of 70, while the incidence is lower in Chinese, Japanese and African–Americans.[3,4]

The onset of AGA typically occurs between 30–40 years of age, although recent studies have shown that it can begin as early as immediately after puberty.[5–7] AGA in patients $\leq$35 years old is termed early-onset AGA.[8] Clinical studies have shown that early-onset AGA is associated with being overweight (body mass index [BMI] $>$ 25 kg/m^2),[9] metabolic syndrome,[10] insulin resistance,[8] cardiovascular diseases[11] and a family history of AGA.[12] However, data on early-onset AGA in the Chinese population remain unpublished. This current study characterized the demographic and clinical features of early-onset AGA in a large cohort of patients in China.

Patients and methods

Study population

This descriptive study searched the Clinical Database of Hair Diseases (Veeva Systems Inc., Pleasanton, CA, USA) to identify all patients receiving treatment for clinically diagnosed early-onset AGA between 1 January 2013 and 30 November 2018 in the Department of Dermatology at the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China. Patients were consecutively recruited if they reported being no older than 35 years when their AGA symptoms began and if their pattern of hair loss was documented with photographs. Patients were excluded if they had been diagnosed with other hair diseases, including telogen effluvium, diffuse alopecia areata, frontal fibrosis alopecia and drug-induced alopecia.

This study was approved by the Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University (no. 2019-SRFA-149). As this was a retrospective analysis, all study participants provided verbal informed consent for the use of their data for research purposes on the condition that the data were anonymized.

Demographic and clinical characteristics

The following demographic and clinical information were collected for each individual: sex, age at AGA onset, date of first visit to the hair-loss clinic, BMI, severity of hair loss and family history of AGA. BMI was

calculated as the square of the body weight divided by body height according to the medical records from the patient's first visit. Overweight was defined as BMI $\geq$25 kg/m^2.[13]

AGA diagnosis

Androgenetic alopecia was diagnosed based on recession of the frontal temporal hair line and hair thinning over the frontal and/or vertex areas in men; and diffuse thinning involving the frontal and vertex scalp in women, as supported by photograph(s). The severity of AGA at the patient's first visit to the hair-loss clinic was assessed by a senior hair dermatologist (W-X.F.). Patterns of male and female AGA were evaluated using the BAsic and SPecific (BASP) classification systems (Figure 1).[14,15] The BAsic classification measures the pattern of hair loss, while the SPecific classification measures the area of hair loss. Classifications of $M_{1–2}$, C_1, $V_{1–2}$ and $F_{1–3}$ were defined as mild/moderate AGA; M_3, C_2 and V_3 as moderate/severe AGA; and C_3 and $U_{1–3}$ as severe AGA.[14,15] Handheld dermoscopes (Heine Delta 20, Heine Optotechnik, Herrsching, Germany; Fotofinder Handyscope, FotoFinder, Bad Birnbach, Germany) were used to determine the diameter of the hair strands, hair density and vellus on the susceptible scalp. AGA was defined as having $>20\%$ heterogeneity in hair shaft thickness and $>20\%$ vellus in the same view (Figure 2).[16]

Statistical analyses

All statistical analyses were performed using the SPSS® statistical package, version 17.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Data are presented as

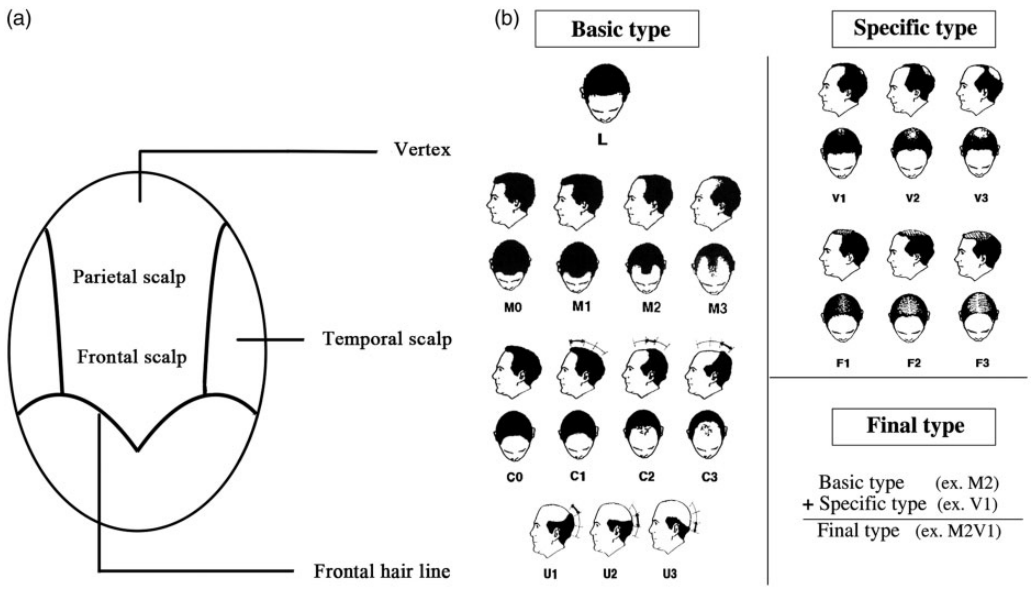

Figure 1. Anatomical regions of the scalp (a). The BAsic and SPecific classification systems (b). Four BAsic types (L, M, C and U) and two SPecific types (frontal [F] and vertex [V]). L, no recession is observed in the frontotemporal region; M, recession in the frontotemporal hairline is more obvious than the mid-anterior hairline; C, recession in the mid-anterior hairline is more obvious than the frontotemporal hairline; U, the anterior hairline recedes to the vertex forming a horseshoe shape.[14,15]

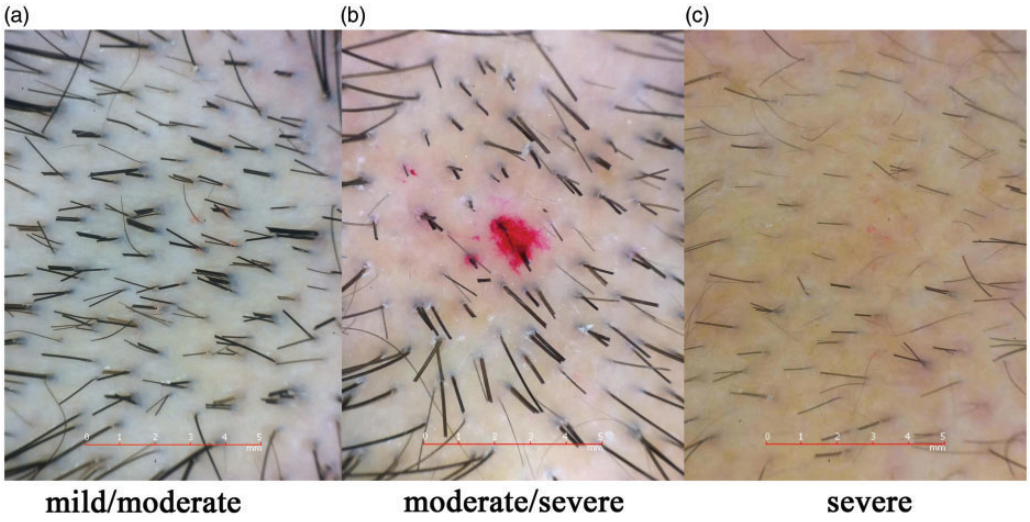

Figure 2. Dermoscopic photographs showing representative images of the different stages and severities of androgenetic alopecia used in this current study.

mean ± SD or *n* of patients (%). Categorical data were analysed using χ^2-test. A *P*-value < 0.05 was considered statistically significant.

Results

This descriptive study analysed data from 3897 patients with early-onset AGA. Of these patients, 2834 (72.7%) were male and 1063 (27.3%) were female. The mean ± SD age was 26.0 ± 4.6 years, with a minimum age of 13 years (range, 13–35 years). The age and sex distribution of early-onset AGA patients is shown in Figure 3. The majority of patients (70.6%; 2751 of 3897 patients) were 21–30 years old and 428 patients (11.0%) were ≤20 years old. Men predominated in all age intervals.

The mean ± SD BMI was 23.2 ± 2.9 kg/m^2 in male patients and 21.1 ± 3.0 kg/m^2 in female patients. Of the 3685 patients for whom BMI was known, 728 (19.8%) were overweight (BMI ≥ 25 kg/m^2). Of the overweight patients, 86.8% (632 of 728 patients) were men and 13.2% (96 of 728 patients) were women ($P < 0.001$; Figure 4).

Of the 3897 patients with early-onset AGA, 2978 (76.4%) were classified as having mild/moderate AGA, while 817 (21.0%) had moderate/severe AGA and 102 (2.6%) had severe AGA.

A total of 2837 (72.8%) of 3897 patients with early-onset AGA had a family history of AGA: 1498 (52.8%) with a paternal history only; 688 (24.3%) with a maternal history only; 612 (21.6%) with both a paternal and maternal history; and in the remaining 39 cases (1.4%), one or more siblings but none of their parents had AGA. In total, 2112 of the 2834 male patients (74.5%) and 725 of the 1063 female patients (68.2%) had a family history of AGA (Figure 5).

Discussion

Androgenetic alopecia is the most common genetic non-scarring skin disease and it typically begins between 30 and 40 years of age.[3] The prevalence of AGA is around

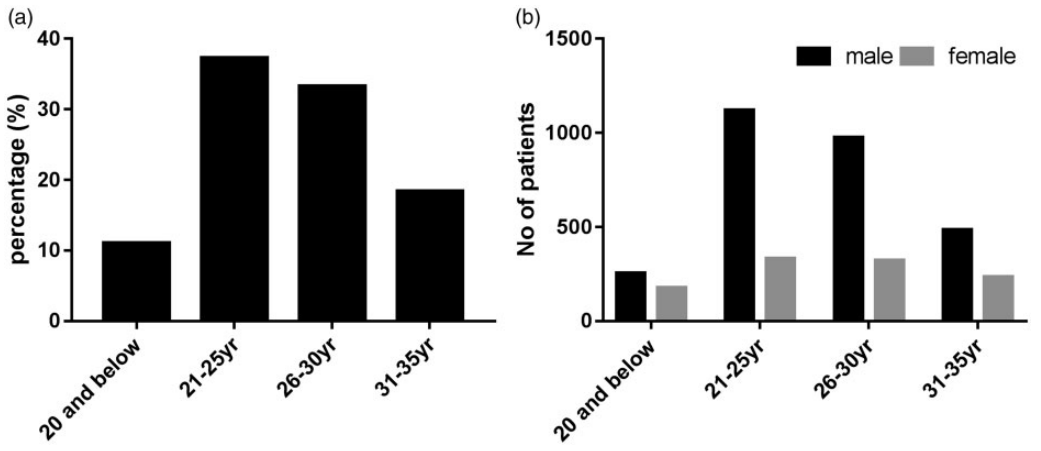

Figure 3. Age distribution of patients with early-onset androgenetic alopecia (a). Comparison of the sex of patients with early-onset androgenetic alopecia according to the age distribution (b).

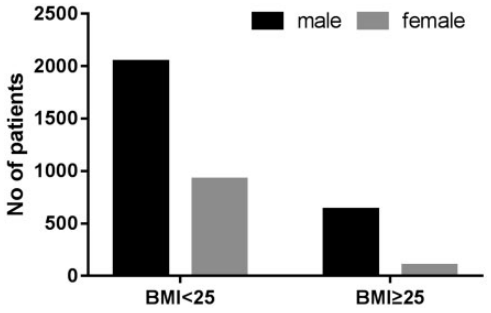

Figure 4. Body mass index (BMI) of male and female patients ($n = 3685$) with early-onset androgenetic alopecia.

30% in male Caucasians in their 30s and it increases to 40% among men aged 50 years.[17] Moreover, AGA affects up to 30% of postmenopausal women.[2] A population-based cross-sectional study in China reported that 19.9% of men had AGA and 0.1% of women had female-pattern alopecia.[18] Several recent studies identified cases of early-onset AGA, but the sample sizes were too small to evaluate the characteristics of the disease.[5,6,19] In this current study, early-onset AGA mainly affected individuals aged 21–30 years old, in accordance with a previous study on adult Caucasian males.[20] Previous studies reported a lower incidence of AGA in women than men.[18,21] These current data show that early-onset AGA is also more likely to affect males than females.

A previous 5-year clinical study in South Korea included 43 adolescent AGA patients.[6] This current study has substantially more power, with more adolescent AGA subjects, the youngest being 13 years old. These current findings suggest that early-onset AGA could be attributed to the early onset of puberty. Further studies will be required to determine whether this is the case.

Previous studies have found contradictory results on the relationship between BMI and AGA. For example, two studies reported that a high BMI was associated with more severe AGA in a Caucasian population[22] and in early-onset AGA cases in Taiwan.[19] However, a third study concluded that BMI does not correlate with AGA onset at any age.[23] In this current study, 80.2% of AGA patients had a normal BMI; and there was no association observed between early-onset AGA and

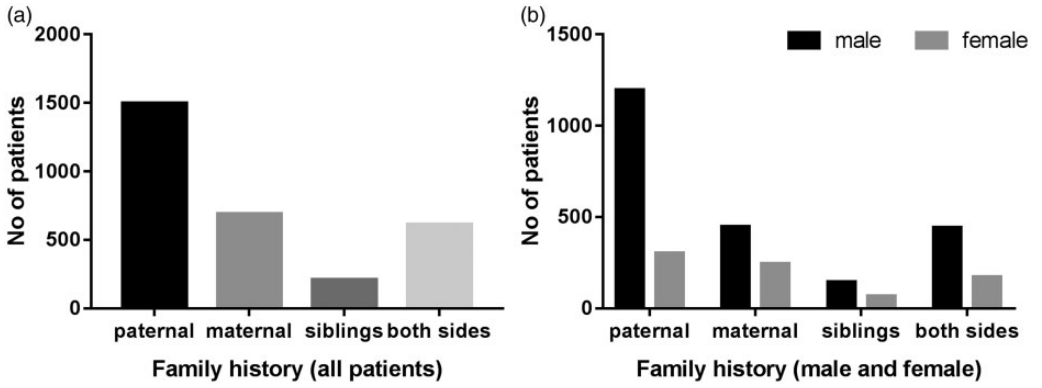

Figure 5. Distribution of patients according to their family history of androgenetic alopecia (a). Comparison between the sexes of a positive family history of androgenetic alopecia (b).

being overweight in men. The majority of overweight patients in this current study were male (86.8% versus 13.2%). This may have been because there were many more male than female AGA patients in this current sample and it may also reflect higher incidence of early-onset AGA in males than females.

In this current study, the majority (76.4%) of patients with early-onset AGA had mild/moderate AGA. This may be because younger AGA patients are more likely to seek immediate treatment. In our hair-loss clinic, it has been observed that early treatment is crucial for a better therapeutic outcome.

Androgenetic alopecia is thought to be a polygenic trait, but the exact pattern of inheritance has not been determined.[24] An epidemiological study of 3114 Korean patients with AGA revealed that 64.1% (1207 of 1883 patients) of male patients and 49.4% (608 of 1231 patients) of female patients had a positive family history of AGA.[25] In contrast, a study in China found that only 29.7% of males and 19.2% of females with AGA had a family history of AGA.[26] In the present study, 72.8% of early-onset AGA patients had a family history of the disease. There were nearly twice as many patients with a paternal history of AGA than those with a maternal history, and 21.6% of patients had both a paternal and a maternal history of AGA. These current results suggest that a family history of AGA, especially on the paternal side, plays an important role in early-onset AGA. Consistent with this, a study in South Korea reported that paternal AGA had a greater effect on AGA expression than maternal AGA.[27] Previous studies have found that AGA predisposition can be inherited from the paternal, maternal, or both sides. For example, a Korean outpatient-based study, which included 1218 AGA patients, found that paternal inheritance was common in both male and female patients.[28] Another South Korean study observed that family history was associated with earlier AGA onset and severity of hair loss.[29] Indeed, some studies have suggested that genetic variability in the androgen receptor on the X chromosome seems to be the primary driver of early-onset AGA,[30,31] while other work has suggested that autosomal loci associated with AGA susceptibility may explain the similar AGA development between fathers and sons.[30,31] Interestingly, the South Korean study noted that family history

appeared to influence BASP classification differently in male and female AGA patients: parental family history influenced the anterior hairline shape in males but less so in females.[29] Further studies will be needed to elucidate the exact polygenic mode of inheritance in early-onset AGA.

Currently, minoxidil and finasteride are the most frequently used treatments approved by the US Food and Drug Administration. However, research continues into new treatments. For example, platelet-rich plasma, which can heal hidradenitis suppurativa and wounds in soft and hard tissue,[32–34] may be an effective AGA treatment.[35] Human autologous follicle stem cells and grafts have also been used to treat AGA.[36–39] A Chinese study has suggested that AGA-associated long non-coding RNAs and their target genes may serve as promising therapeutic targets for preventing and treating AGA.[40] Further studies will be needed to confirm the efficacy and safety of these treatments.

This current study had several limitations. First, all of the patients were recruited from a single medical centre and may not necessarily reflect the characteristics of early-onset AGA in the general population. Secondly, the study did not conduct any genetic analyses as it was only descriptive. Thirdly, since the age of AGA onset in this current study was based on patient self-report, it may have overestimated the actual age at symptom onset.

Despite these limitations, this current large study provides strong evidence that early-onset AGA is more frequent in males than females in China. It also suggests that paternal inheritance plays a greater role in the development of early-onset AGA than either maternal inheritance or the combination of maternal and paternal inheritance.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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ORCID iD

Wei-Xin Fan https://orcid.org/0000-0001-6328-0490

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