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The Use of 2D:4D Digit Ratio as a Predictor of Androgenetic Alopecia: A Review

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ABSTRACT Androgenetic alopecia (AGA) is a widespread type of hair loss that affects both males and females. Advanced age and family history of AGA are well-established risk factors for developing AGA. The second to fourth digit ratio (2D:4D) is the ratio between the length of the index and ring fingers. This ratio has been utilized as a predictor for multiple hyperandrogenism-related medical conditions. More recently, 2D:4D was investigated as a predictor for AGA. This article aims to investigate the evidence supporting the use of 2D:4D as a predictor of AGA, and address areas of future research.

Introduction

Androgenetic alopecia (AGA) is a prevalent type of hair loss affecting both males and females. It impacts roughly eighty percent and fifty percent of males and females, respectively [1,2]. Androgens shorten the anagen phase of the hair follicle, which, in turn, leads to a reduction in its size and miniaturization of the hair—the hallmark of AGA [3-5].

Furthermore, androgenetic alopecia can have many psychological repercussions including low self-esteem, low mood, anxiety, and social withdrawal [6,7]. Moreover, advanced age and genetic susceptibility, including family history of AGA are all well-recognized risk factors for AGA [8,9].

A recently emerging indicator for the identification of different medical conditions is the second-to-fourth digit ratio, also known as the 2D:4D. The second to fourth digit

ratio (2D:4D) is the ratio between the length of the index and ring fingers. This ratio has been utilized to predict the risk of hyperandrogenism, high body mass index and waist-to-hip ratio, and benign prostatic hyperplasia [10-12].

Recent studies have investigated the potential of the 2D:4D as a predictive factor for AGA. It is postulated that a lower 2D:4D ratio may signify elevated levels of perinatal testosterone, thereby serving as an indicator for an increased likelihood of developing AGA [13,14]. This article aims to investigate the evidence supporting the use of 2D:4D as a predictor of AGA, and address areas of future research.

Methods

A comprehensive literature search was conducted in the Medline and Google Scholar databases from their commencement until February 2023. The search combined terms related to the second-to-fourth digit ratio ("Second-to-fourth digit ratio OR "2D:4D ratio" OR "Digits") and androgenetic alopecia ("Androgenetic alopecia" OR "Androgenic alopecia" OR "AGA"). There were no language restrictions. Additionally, references of included articles and relevant reviews were manually searched for additional studies. A total of four articles were identified that specifically examined the value of the 2D:4D in predicting the risk and severity of androgenetic alopecia.

Results

Few studies have been conducted to specifically assess the association between a low 2D:4D and a higher risk of developing AGA (Table 1). The most recent of which was a cross-sectional study conducted by Chen et al. in 2022, which included 240 patients with varying degrees of AGA severity. The authors found that individuals with a right-hand 2D:4D less than 0.947 (index finger shorter than ring finger) may have a more severe form of AGA (P = 0.036). Nonetheless, factoring in patients' age as a predictor for AGA risk alongside the 2D:4D was shown to be superior to either predictor alone, resulting in an odds ratio of 6.1, as opposed to 2.8 when 2D:4D is used by itself [15].

To this date, a single-center, descriptive, analytical study involving 1200 Iranian men is the largest and most controlled study conducted to assess the association between digit length and AGA risk. The study sample was selected using random sampling and was stratified based on the severity of

Table 1. Summary of the studies conducted to assess the association between Second-to-fourth digit ratio and androgenetic alopecia.

Study	Study design	Sample size (N)	Mean patient age in years (SD)	Results
Chen et al, 2022 [15]	Cross-sectional study[a]	240	32.9 (8.4)	Significant association between low 2D:4D of the right hand and higher grade of AGA (P = 0.036). Significant association between older age and a higher grade of AGA (P = 0.006).
Unal, 2018 [19]	Case-control study[a]	189 (Case and control groups included 99 and 90 patients, respectively)[b]	Case group: 29.7 (5.5). Control group: 19.6 (5).	Significant association between low 2D:4D of the left hand and having AGA (P < 0.001). No significant relationship between 2D:4D and the severity of AGA in either the left or right hands.
Bilgic et al, 2016 [20]	Cross-sectional study[a]	360 (Case and control groups included 189 and 171 patients, respectively)[b]	Not stated.	Significant association between low 2D:4D of the right hand and having AGA (P < 0.001). No significant relationship between 2D:4D and the severity of AGA in either the left or right hands.
Feily et al, 2016 [16]	Single-site, descriptive-analytical study[a]	1200	33.2 (0.28)	No significant association between low 2D:4D of the right (P = 0.747) or left (P = 0.337) hand and having AGA. Positive correlation coefficient identified between low 2D:4D and AGA only in individuals older than 40 years of age.

AGA = Androgenic alopecia; SD = standard deviation;2D:4D: Second-to-fourth digit ratio.

[a]Norwood scale was used to assess the severity of AGA. Second- and fourth-digits length was measured using a digital vernier caliper.
[b]Patients with AGA grades I and II have been excluded from the study.

AGA using the Hamilton-Norwood scale. The authors found no significant association between the- right and left-hand 2D:4D. There was, however, a positive correlation between a low 2D:4D and the risk of AGA, but only in those older than 40 years of age [16]. According to their findings, the 2D:4D may not be used to determine a patient's likelihood of developing AGA without also considering the patient's age.

While the largest study showed no link between the digit ratio and AGA risk [16]. The findings of the other three studies consistently demonstrate that the 2D:4D can be used to predict the likelihood of developing AGA, particularly when combined with age in the context of risk evaluation.

Combining Age With the 2D:4D for the Prediction of AGA Risk

Even though previous research demonstrates a degree of inconsistency when it comes to using the 2D:4D by itself to assess the risk of AGA (Table 1), it is abundantly apparent that if the ratio is to be used to evaluate an individual risk, combining it with age provides predictions that are significantly more accurate.

Right Versus Left-Hand 2D:4D

The subject of the right-hand versus left-hand 2D:4D susceptibility for testosterone levels has been investigated in a number of different studies. The 2D:4D of the right hind paw was discovered to be more responsive to embryonic androgens than the left hind paw ratio in a research carried out on mice [17].

In humans, a study conducted by Manning et al were the authors concluded that the 2D:4D was more sensitive to testosterone and estrogen levels and would therefore be a better reflector of prenatal androgen exposure than that of the left hand [18]. Similar findings were also reported by Hönekopp et al, were they conducted a meta-analysis to describe the effect of gender on the 2D:4D ratio and found that males have a lower 2D:4D of the right hand than females; the left hand showed no statistically significant difference among genders [14].

Conclusions

There have been a limited number of studies conducted on the use of 2D:4D as a predictor of AGA risk; therefore, it is still not entirely clear whether the second-to-fourth-digit finger ratio is a reliable predictor of AGA risk when used in isolation. However, taking the 2D:4D into consideration along with the patient's age seems to improve the prediction accuracy of either factors alone. While further controlled studies are needed to confirm these results, this study provides evidence that there may indeed be a link between digit ratios and susceptibility to AGA.

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