Digit-length ratios (2D:4D) as a phenotypic indicator of *in utero* androgen exposure is not prognostic for androgenic alopecia: a descriptive-analytic study of 1200 Iranian men.

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Abstract

The etiology of androgenic alopecia (AGA) involves several factors, including genetics, androgens, age and nutrition. Digit-length ratio of the index and ring finger (2D:4D) is an indicator of prenatal exposure to sex hormones. There is a paucity of studies that systemically review the possible positive predictive value of 2D:4D in the development of AGA. We performed a single-site, descriptive-analytical study among a racially homogeneous population. Our results revealed that no significant association was determined between right 2D:4D and AGA severity within our entire population (P=0.384, r=0.025), however a positive correlation coefficient was identified in subjects above the age of 40. Based on the receiver operating characteristic curve analysis, 2D:4D does not predict the development of AGA. AGA is truly a multifactorial disease. Further, our findings suggest that increased *in utero* exposure to androgens as a fetus does not predispose men to develop AGA.

Introduction

Androgenic alopecia (AGA) is the most common type of progressive hair loss. The etiology of AGA involves several factors, including genetics, androgens, age and nutrition.[1-4] Some evidence suggests that the digit-length ratio of the index and ring finger (2D:4D) is an indicator of prenatal exposure to sex hormones, with a lower 2D:4D being suggestive of a greater androgen exposure.[5-8]

Digit-length ratios have been utilized to determine the effects of prenatal androgen exposure a variety of phenotypic expressions.[5,6,8] However, there is a paucity of studies that systemically review the possible positive predictive value of 2D:4D in the development of AGA.

Materials and Methods

The study was initiated after approval by the research and ethics committee of Jahrom University of Medical Sciences, approval ID: JUMS.REC.1393.017. All participants signed an informed consent prior to participating in the study. We performed a single-site, descriptive-analytical study between June 2013 and February 2014 among a racially homogeneous population that they were selected by stratified and randomized sampling. Participants did not have a significant history of other types of alopecia (*e.g.* iatrogenic scarring alopecia, alopecia areata, *etc.*). A trained team performed digit-length measurements of both hands with vernier calipers and subsequently calculated the 2D:4D. A single trained technician graded baldness using the Hamilton-Norwood Classification scale; for simplicity these grades were further divided into four stages: no baldness (I), mild (II, III), moderate (IV, V) and severe baldness (VI, VII).

Associations between 2D:4D and AGA were determined with SPSS version 16. The quantitative results are presented as a mean±standard deviation (SD). A Pearson linear correlation was performed to assess relationships between 2D:4D and age; a Spearman linear correlation to assess relationships between 2D:4D and AGA severity, and ROCs mode was used to measure the validity of 2D:4D as a predictive test for AGA. Statistical significance was assigned at P<0.05.

Results

A total of 1200 men between 20 to 60 years of age with a mean age of 33.2 (SD: 0.28), enrolled in the study. The prevalence of AGA among the study population was 45.4%. A total of 53.4% of the participants had normal hair distribution (aged 29.95±8.4 years), 26.16% had mild hair loss (aged 34.97±10.11 years), 15.19% had moderate (aged 40.35±9.43 years) and 4.32% had severe hair loss (aged 42.28±9.92 years).

The mean ratio of the right 2D:4D was 0.992 (SD: 0.0024), while the left was 0.982 (SD: 0.0017). No significant differences were identified between left and right hand 2D:4D per subject (Table 1). There was significant association between age and AGA(r=-0.426, P=0.001). No significant association was determined between right 2D:4D and AGA severity within our entire population (P=0.384, r=0.025), also there was no significant association between left 2D:4D and AGA severity (P=0.495, r=0.028), however a correlation coefficient was identified in subjects above the age of 40.

The receiver operating characteristic (ROC) analysis of subjects age 40 and above demonstrated the area under curve (AUC) as 0.502 (95%CI 0.391 to 0.613) and 0.480 (95% CI 0.371 to 0.590) for right and left 2D:4D, respectively, as a predictive test for AGA (Figure 1).

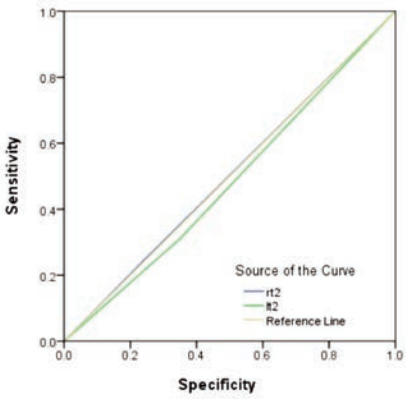

Figure 1. Receiver operating characteristic curve analysis of right and left 2D:4D with androgenetic alopecia gold standard.

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Table 1. Mean of 2d:4d ratio compared to androgenetic alopecia stage severity.

AA stages	Mean	SD	95% CI	Sum of squares	Df	Mean square	F	Sig.
Right ratio				0.009	3	0.003	0.409	0.747
Normal	0.9919	0.08179	0.9855-0.9982					
Mild	0.9952	0.06994	0.9874-1.0030					
Moderate	0.9913	0.09576	0.9770-1.0057					
Severe	0.9810	0.13942	0.9391-1.0229					
Left ratio				0.012	3	0.004	1.127	0.337
Normal	0.9853	0.06019	0.9806-0.9899					
Mild	0.9781	0.04175	0.9735-0.9828					
Moderate	0.9795	0.09040	0.9659-0.9931					
Severe	0.9812	0.03508	0.9707-0.9918					

AA, androgenetic alopecia; SD; standard deviation; CI, confidence interval.

Discussion and Conclusions

Herein, is the largest study to date aimed to explore the utility of a phenotypic expression of *in utero* androgen exposure in predicting the development of AGA. The prevalence of AGA was 45.4%, similar to worldwide reports.[9,10] The prevalence of AGA trended upwards as participant age increased. Although there was no significant association between right 2D:4D and AGA (P=0.384, r=0.025), there was a correlation coefficient identified in subjects above the age of 40. With increasing of age the AGA severity increases especially in participants above the age of 40.

In clinical practice, most patients generally express AGA by age 40. Therefore, we attempted to evaluate the utility of 2D:4D as a predictive test for AGA. Based on the ROC curve analysis, 2D:4D does not predict the development of AGA. AGA is truly a multifactorial disease. Further, our findings suggest that increased *in utero* exposure to androgens does not predispose men to develop AGA.

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