



## ORIGINAL ARTICLE

## The Clinical Differences on 2:4 Finger Ratios of the Hirsute Women

Raziye Desdicioglu<sup>1\*</sup>, Fatma Betul Erdemli<sup>1</sup>, Selma Caliskan<sup>2</sup>, Kadir Desdicioglu<sup>2</sup> and Ayse Filiz Yavuz<sup>1</sup>



<sup>1</sup>Medical Faculty, Department of Obstetrics and Gynecology, Ankara Yıldırım Beyazıt University, Ankara, Turkey

<sup>2</sup>Medical Faculty, Department of Anatomy, Ankara Yıldırım Beyazıt University, Ankara, Turkey

\*Corresponding author: Dr. Raziye Desdicioglu, Medical Faculty, Department of Obstetrics and Gynecology, Ankara Yıldırım Beyazıt University, Ankara, Turkey, Tel: +90-312-324-1555, Fax: +90-312-324-1518

### Abstract

**Background:** We aimed to research whether there was a difference in terms of the 2:4 finger ratio between women with hirsutism and healthy women without hirsutism and the correlation between degree of hirsutism and 2:4 finger ratios and clinically evaluated our results.

**Methods:** Our study included 144 voluntary women (control group: 51, study group: 93) with ages from 18 to 38 years. The hirsutism level of patients was assessed using the Ferriman-Gallway scale with points given from 0 to 4 in 9 body regions. All patients in the study and control groups had measurements of both hands measured by the same research with a digital calipers sensitive to 0.01 mm (INSIZE). The serum total testosterone levels and Dehydroepiandrosterone (DHEAS) of patients in the study group were biochemically studied. Additionally the age, height and weight values for all patients were recorded in the study.

**Results:** The length of the 2<sup>nd</sup> finger of the right hand in the control group was larger compared to the study group and this difference was identified to be significant (control group 68.40 ± 5.37, study group 65.72 ± 4.94 p = 0.02). Though the right and left hand 2:4 finger ratios were higher in the control group, comparison between the groups did not identify a statistical difference (control group: 0.98 ± 0.05 mm; study group: 0.97 ± 0.06 mm p = 0.8). There was no significant correlation observed between degree of hirsutism and parameters measured on the hands.

**Conclusions:** The results of our study found that patients with hirsutism may have increased androgen exposure in fetal life or in the adult period and leads to the consideration that this situation may be effective in the etiopathogenesis of hirsutism.

### Keywords

2:4 finger ratio, Hirsutism, Polycystic ovarian syndrome

### Introduction

Hirsutism affects 5-10% of women of reproductive age and is defined as excessive terminal hair in regions of the body sensitive to androgen like the face, chin and upper lip [1]. It is characterized by reduced quality of life and disrupted self-image. The causes of hirsutism may be androgenic, non-androgenic and idiopathic. The most common causes are androgenic and mainly involve polycystic ovarian syndrome (PCOS) [2]. PCOS affects 4-12% of women of reproductive age and is a metabolic disease characterized by anovulation and hyperandrogenism [3]. For diagnosis the Rotterdam criteria comprising criteria like oligo-amenorrhea, polycystic ovarian appearance on ultrasonography with 10 or more follicles with peripheral localization and size of 2-8 mm, and clinical or laboratory ovarian hyperandrogenism [4]. Clinically hyperandrogenism is associated with hirsutism, acne and male-type alopecia [3]. Additionally, biochemically hyperandrogenism is characterized by high serum total testosterone and dehydroepiandrosterone (DHEAS) levels [3]. Congenital adrenal hyperplasia is responsible for a portion of androgenic causes [1]. Of hirsutism cases, 6-15% are classified in the idiopathic hyperandrogenism category. Diagnosis and degree of hirsutism uses the modified Ferriman-Gallway scale assessing the density of hairs in

9 regions of the body. This scale gives points from 0 to 4 for density of hair present in these regions. When a score of 6 or more is accepted as hirsutism, it is thought to include 95% of cases [5].

It is thought that the hand 2:4 finger ratio is related to androgen exposure during prenatal life and personal androgen sensitivity [6,7]. In the human fetus, hair follicles begin to be seen from about the 9th week of pregnancy and the majority have developed by the 16th week of pregnancy. This period is also stated to be the period when finger development is affected by androgen exposure [8,9]. Some studies have stated that bone development in the fetal period is related to hormones and this correlation may indicate some diseases [10,11]. It is known the 2:4 finger ratio is high in women. Robinson, et al. [10] stated the 2:4 finger ratio showed positive correlation with estrogen and negative correlation with testosterone in their study. There are studies showing the 2:4 finger ratio is affected in situations like congenital adrenal hyperplasia with increased androgen exposure and XY individuals with androgen insensitivity [8]. Experimentally, the offspring of pregnant rats with changed androgen levels had 2:4 finger ratio affected [8]. Additionally, there are studies stating that androgen receptor gene polymorphism is related to 2:4 finger ratio [8,12,13].

In situations related to androgen metabolism like acne vulgaris, alopecia areata and skin sebum levels, previous studies have shown a relationship with 2:4 finger ratio [14-16]. We did not encounter any research investigating the correlation between hirsutism and 2:4 finger ratio. Different to other studies, in our study we aimed to research whether there was a difference in terms of the 2:4 finger ratio between women with hirsutism and healthy women without hirsutism and the correlation between degree of hirsutism and 2:4 finger ratios and clinically evaluated our results.

## Methods

Our study included 144 voluntary female patients (control group: 51, study group: 93) who applied to the Ankara Yıldırım Beyazıt University Atatürk Education and Research Hospital Gynecology and Obstetrics clinic with ages ranging from 18 to 38 years. Female patients in the control group applied to the gynecology clinic for any complaint and were chosen from patients who did not abide by the exclusion criteria. Female patients in the study group included patients applying for increased hair, with PCOS diagnosis and modified Ferriman-Gallway score of 6 and above. For PCOS diagnosis the Rotterdam criteria were used [4]. From these diagnostic criteria, oligo-anovulation is defined as menstrual dysfunction characterized by 6 or fewer menstrual periods per year. The PCOS appearance is defined as visualization of 12 or more follicles with a diameter of 2-9 mm at each ovary with transvaginal ultrasound on the 2<sup>nd</sup>-5<sup>th</sup> days of menstruation. Patients

who did not wish to participate, pregnant cases, those with hypertrichosis, patients using medication that may cause increased hairiness (steroids, etc.) and patients with causes of hirsutism other than PCOS were excluded from the study. Additionally permission for the study was granted by Ankara Yıldırım Beyazıt University Atatürk Education and Research Hospital Clinical Ethics Committee (Approval Number 185, Approval date 25/10/2017).

Patients in the study group had hirsutism levels assessed with the modified Ferriman-Gallway scale with points from 1-4 given for 9 regions of the body [5]. All patients in the study and control group had measurements of both hands measured by the same researcher using a digital calipers sensitive to 0.01 mm (INSIZE). On both hands the lengths of the 2<sup>nd</sup> and 4<sup>th</sup> fingers were measured between the bottom of the finger (from the proximal curve of the metacarpophalangeal joint on the volar face) and the end point as the longest vertical distance on a flat surface [17]. Hand length used the vertical distance from the curve of the wrist to the topmost point of the middle finger, while hand width was measured as the widest transverse distance between the outer edges of the 2<sup>nd</sup> and 5<sup>th</sup> metacarpal bones [17]. Additionally the hand index and body mass index (BMI) values were determined for patients in the study and control groups (hand index: (hand width/hand length) × 100, BMI: Body weight/height<sup>2</sup>) [17]. Patients in the study group had serum androgen levels assessed in the early proliferative period of the cyclus (2-5 days) after 12 hours starvation. Serum total testosterone levels and DHEAS levels were studied biochemically. Additionally patients in the study and control groups had age, weight and heights recorded in the study.

For statistical analysis the SPSS version 20 was used in the study. Normal distribution of data was assessed with the Kolmogorov-Smirnov test. The t-test was used to assess differences between the two groups. Pearson correlation analysis was used for correlation analysis. The paired t-test was used to compare differences between the right and left hands of patients.

## Results

The mean age of the 74 volunteers in the control group was 25.88 ± 5.50, with mean age in the volunteer study group 23.70 ± 5.70 years. In our study the 2<sup>nd</sup> and 4<sup>th</sup> finger lengths, 2:4 finger ratios, hand length and width and hand index of the right and left hands were determined in the control and study group. Comparison of the 2<sup>nd</sup> finger lengths on the right and left hands between the groups found a statistical difference ( $p < 0.05$ ), while comparison of 2<sup>nd</sup> finger lengths on the right and left hands within the groups found a statistical difference in the study group ( $p < 0.05$ ) while there was no difference in the control group ( $p > 0.05$ ). Comparisons of the 4<sup>th</sup> finger lengths on the right and

**Table 1:** Comparison of parameters between the two groups.

Parameters	Control (51)	Patient (93)	p
Age	25.88 ± 5.50	23.70 ± 5.43	0.02
BMI	23.34 ± 3.82	24.97 ± 5.73	0.04
Modified Ferriman-Gallway Score	3.90 ± 1.08	15.11 ± 6.52	0.000
Right hand 2nd finger length (mm)	68.40 ± 5.37	65.72 ± 4.94	0.02
Right hand 4th finger length (mm)	69.75 ± 4.58	68.34 ± 4.87	0.05
Right hand 2:4 finger ratio (mm)	0.98 ± 0.05	0.97 ± 0.06	0.8
Left hand 2nd finger length (mm)	69.25 ± 4.84	67.21 ± 4.79	0.01
Left hand 4th finger length (mm)	67.78 ± 4.900	66.81 ± 5.33	0.02
Left hand 2:4 finger ratio (mm)	1.02 ± 0.04	1.00 ± 0.07	0.2
Right hand 2:4 finger ratio/Left hand 2:4 finger ratio (mm)	-0.04 ± 0.09	-0.03 ± 0.1	0.5
Comparison of the 2nd finger lengths on the right and left hands	68.40 ± 5.37-69.25 ± 4.84	65.72 ± 4.94-67.21 ± 4.79	0.010
Right hand width (mm)	76.43 ± 4.56	76.17 ± 5.84	0.1
Right hand length (mm)	167.29 ± 8.53	167.30 ± 6.85	0.7
Left hand width (mm)	76.93 ± 4.36	75.75 ± 5.05	0.1
Left hand length (mm)	167.70 ± 7.96	167.32 ± 7.86	0.7
Right hand index (mm)	50.38 ± 0.28	47.88 ± 0.19	0.00
Left hand index (mm)	50.76 ± 0.30	47.94 ± 0.20	0.00

p < 0.05: Significant difference between groups; p > 0.05: No significant difference between groups.

left hands between the groups and within the groups determined a statistical difference (p < 0.05). Though the right and left 2:4 finger ratios were higher in the control group, there was no statistical difference identified during comparisons between and within the groups (p > 0.05). Comparisons of the right and left hand lengths and widths between the groups and within the groups did not determine a statistical difference (p > 0.05). Comparison of right and left hand indices between the groups was statistically significant (p < 0.00), while comparison within groups was not identified to be statistically significant (p > 0.05). Parameter data for the groups and detailed comparisons of parameter data are summarized in [Table 1](#).

Our study also obtained data about the modified Ferriman-Gallway score, age, BMI, DHEAS and total testosterone levels. Comparison of modified Ferriman-Gallway score, age and BMI values between the groups was statistically significant (p < 0.05) with no significance for comparisons within the groups (p > 0.05, [Table 1](#)). Additionally, correlation analysis observed a positive correlation between modified Ferriman-Gallway score and DHEAS and BMI ([Table 2](#)). Apart from right and left 2:4 finger ratios and right and left hand indices, the parameters of both hands appeared to be correlated with age ([Table 2](#)). There was a positive correlation observed between BMI and the width values for both hands ([Table 2](#)). There was no correlation observed between the modified Ferriman-Gallway scores and both hand 2:4 finger ratios of patients ([Table 2](#)). Additionally no significant correlation was observed between total testosterone levels and modified Ferriman-Gallway score ([Table 2](#)). Correlation analysis of parameters is summarized in [Table 2](#).

## Discussion

Hirsutism is defined as excessive terminal hairs in androgen-sensitive regions of the body like the face,

chin and upper lip [1]. Diagnosis and degree of hirsutism uses the modified Ferriman-Gallway scale assessing the density of hairs in 9 regions of the body. In the human fetus, hair follicles begin to be seen from about the 9th week of pregnancy and the majority has developed by the 16th week of pregnancy. This period is also stated to be the period when finger development is affected by androgen exposure [8,9]. Additionally, there are studies stating the hand 2:4 finger ratio is related to androgen exposure in prenatal life and personal androgen sensitivity [6,7].

When we examined previous studies related to the 2:4 finger ratio, we did not encounter any study researching the correlation between hirsutism and 2:4 finger ratio. Studies have investigated the correlation between hirsutism and androgen levels, the correlation between 2:4 finger ratio and acne vulgaris and alopecia areata, the correlation between 2:4 finger ratio and female sex hormones and the correlation between PCOS and hirsutism [14,15,18,19]. Different to other studies, in our study we aimed to research whether there was a difference in terms of the 2:4 finger ratio between women with hirsutism and healthy women without hirsutism and the correlation between degree of hirsutism and 2:4 finger ratios and clinically evaluated our results.

Firstly in our study we determined the 2nd and 4th finger lengths, 2:4 finger ratios, hand width and length and hand indices for the right and left hand in the control and study groups. The 2nd finger lengths on the right and left hands of the study group were measured shorter compared to the control group and this was determined to be statistically significant (p < 0.05, [Table 1](#)). Additionally comparison of the 2nd finger lengths within the control and study groups found a statistical difference in the study group (p < 0.05), while there was no statistical difference in the control group (p > 0.05).

Table 2: Correlation table showing correlations between parameters.

Age	mFG	BMI	DHEAS	Tt.	HRD <sub>2</sub> L	HRD <sub>4</sub> L	HR2:4	HLD <sub>2</sub>	HLD <sub>4</sub>	HL2:4	HRW	HRL	HLW	HLL	HI <sub>R</sub>	HI <sub>L</sub>
1																
-0.033	1															
0.422*	0.241**	1														
0.068	0.353*	0.102	1													
0.048	-0.007	0.148	0.415**	1												
0.192*	-0.107	0.124	0.130	0.191	1											
0.273**	-0.099	0.066	0.021	0.184	0.673**	1										
-0.061	-0.022	0.088	0.135	0.033	0.548**	-0.249*	1									
0.224**	-0.134	0.132	0.071	0.140	0.667**	0.755**	0.019	1								
0.177*	-0.138	0.107	-0.012	0.134	0.777**	0.572**	0.366**	0.618**	1							
0.045	0.002	-0.011	0.067	0.006	-0.263	0.111	-0.470	0.251**	-0.578**	1						
0.266**	0.022	0.405**	0.062	0.182	0.344**	0.385**	0.008	0.387**	0.348**	-0.014	1					
0.177*	0.033	0.175*	0.027	0.103	0.616**	0.574**	0.160	0.539**	0.544**	-0.086	0.356**	1				
0.189*	-0.135	0.351**	0.096	0.228	0.384**	0.431**	0.009	0.452**	0.404**	0.007	0.786**	0.352**	1			
0.195*	-0.003	0.154	-0.002	0.191	0.631**	0.578**	0.180*	0.504*	0.588**	-0.169*	0.339**	0.931**	0.381**	1		
-0.009	0.053	-0.160	-0.113	-0.150	0.122	0.083	0.064	0.100	0.050	0.043	0.002	-0.046	0.011	-0.047	1	
-0.007	0.052	-0.146	-0.121	-0.159	0.108	0.070	0.059	0.093	0.039	0.049	0.007	-0.052	0.014	-0.052	0.995**	1

\*P < 0.05; \*\*P < 0.01; \*P < 0.05. mFG: Modified Ferriman-Gallway score, BMI: Body mass index; DHEAS: Dehydroepiandrosterone; Tt: Total testosterone; HRD<sub>2</sub>L: Right hand 2nd finger length; HRD<sub>4</sub>L: Right hand 4th finger length; HR2:4: Right hand 2:4 finger ratio; HLD<sub>2</sub>: Left hand 2nd finger length; HLD<sub>4</sub>L: Left hand 4th finger length; HL2:4: Left hand 2:4 finger ratio; HRW: Right hand width; HRL: Right hand length; HLW: Left hand width; HLL: Left hand length; HI<sub>R</sub>: Right hand index; HI<sub>L</sub>: Left hand index.

Comparison of the 4th finger lengths on the right and left found the 4<sup>th</sup> finger lengths were longer in the control group and right hand, with statistical significance identified on comparison between the groups and within the groups ( $p < 0.05$ , Table 1). In our study, additionally, though the 2:4 finger ratios on the right and left hands were higher in the control group, comparison between and within the groups found no significant differences ( $p > 0.05$ , Table 1). Additionally, there was no correlation observed between the modified Ferriman-Gallway scores and total testosterone levels of patients and the finger lengths and 2:4 finger ratios on both hands (Table 2).

When previous studies are examined, a study researching the relationship between the androgen-related situation of acne vulgaris and 2:4 finger ratio showed the right and left 2:4 finger ratios in the acne vulgaris group in women were significantly lower compared to the control group [14]. Another study researched the correlation between skin sebum levels and acne vulgaris in patients with acne vulgaris and showed the presence of a correlation between the sebum levels of the U zone describing the facial region and the left hand 2:4 finger ratio. The same study did not observe a correlation between acne vulgaris severity and 2:4 finger ratio [16]. A study researching the correlation between androgenetic alopecia in males and 2:4 finger ratio showed the right hand 2:4 finger ratio in androgenetic alopecia patients was significantly lower compared to the control group. The same study did not identify a correlation between severity of alopecia and 2:4 finger ratio [15]. The data obtained in our study are in accordance with previous study results. As mentioned in previous studies, exposure to excess androgen in the fetal and adult periods affects bone development and as a result we concluded the 2nd and 4th finger lengths and 2:4 finger ratios in the study group were lower.

Additionally in our study we measured the widths and lengths of both hands and determined the hand indices of both hands. The study results found no significant difference between the control and study groups in terms of hand length and width (Table 1). In terms of hand indices, the control group was higher and we identified a statistically significant difference between the two groups. We did not encounter any study related to these parameters in adult patients (PCOS, hirsutism and acne vulgaris). We interpret the results of our study as showing bone development was affected linked to exposure to androgen amounts in the fetal or adult period.

Later in our study we examined the serum

androgen levels in the study group alone and identified a strong correlation between especially DHEAS levels and degree of hirsutism (rates of 35%) (Table 2). Additionally, we did not observe a correlation between testosterone levels and hirsutism severity. Studies in the literature have shown that clinical and biochemical hyperandrogenism are not always correlated, with 100% clinical hyperandrogenism (hirsutism) cases having testosterone and DHEAS elevation of only 27 to 33% [2]. Studies researching the correlation between adult period androgen levels and 2:4 fingers have shown different results. A meta-analysis investigating many studies concluded that there was no correlation between 2:4 finger ratio indicating prenatal androgen exposure and adult period serum androgens [19]. Another research investigated the correlation between testosterone levels measured after activities increasing peak testosterone levels like watching videos containing aggression and the 2:4 finger ratios. Here, the 2:4 finger ratios were low in the group with excessive testosterone increase. There was no correlation shown between resting testosterone levels and 2:4 finger ratios. The results of our study comply with these results, with no correlation shown between serum androgens and 2:4 finger ratios. We interpret this result as a negative relationship between androgen level and bone development.

Previous research has shown that intrauterine androgen exposure is related to a range of androgenic situations in adult life [12,20]. For example, in situations with congenital adrenal hyperplasia confused sexual thoughts and brain virilization findings were observed independent of treatment [21,22]. Based on this, the correlation between a variety of androgen-related situations in adulthood and 2:4 finger ratio was researched. Some of these showed a correlation between the 2:4 finger ratio and clinical situations [14-16].

Some studies of animal models have investigated the endocrinologic and reproductive results of exposure to excessive androgens in intrauterine life. Research administering external androgens experimentally administered to animals in the early period of pregnancy have shown polycystic ovarian morphology and disrupted menstrual cyclus in some mammal species (pigs, Rhesus monkeys) [23]. A review of these studies stated this was not valid for all mammalian species [23].

Our study limitation is the small number of sample size. Studies based on larger numbers of patients are needed to confirm these findings.

## Conclusion

Our study was performed to investigate the correlation between degree of hirsutism and 2:4 finger ratio. In our study the 2<sup>nd</sup> and 4<sup>th</sup> finger length measurements on both hands of patients with hirsutism and the 2:4 finger ratios were lower compared to the

control group showing these patients had increased androgen exposure in fetal life or the adult period. This leads to the consideration that androgen exposure in the fetal and adult period may be effective in the etiopathogenesis of hirsutism. In conclusion, we believe the results obtained in our study about 2:4 finger ratio data may contribute to clinical practice in the diagnosis of hirsutism and hyperandrogenism. Additionally we believe our study needs to be supported by studies completed with more patients.

## Acknowledgements

The authors would like to thank to the Departments of Obstetrics and Gynecology of the Ankara Atatürk Training and Research Hospital.

## Conflict of Interest

The authors have no conflicts of interest to declare.

## Financial Disclosure

The authors declared that this study has received no financial support.

## References

- Hohl A, Ronsoni MF, Oliveria Md (2014) Hirsutism: Diagnosis and treatment. *Arq Bras Endocrinol Metabol* 58: 97-107.
- Carmina E, Rosato F, Janni A, Rizzo M, Longo RA (2006) Extensive clinical experience: Relative prevalence of different androgen excess disorders in 950 women referred because of clinical hyperandrogenism. *J Clin Endocrinol Metab* 91: 2-6.
- Coskun A, Ercan O, Arikan DC, Özer A, Kilinc M, et al. (2011) Modified Ferriman-Gallwey hirsutism score and androgen levels in Turkish women. *Eur J Obstet Gynecol Reprod Biol* 154: 167-171.
- Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group (2004) Revisited 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Fertil Steril* 81: 19-25.
- Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, et al. (2018) Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod* 110: 364-379.
- Hönekopp J, Bartholdt L, Beier L, Liebert A (2007) Second to fourth digit length ratio (2D: 4D) and adult sex hormone levels: New data and a meta-analytic review. *Psychoneuroendocrinology* 32: 313-321.
- Manning JT (2011) Resolving the role of prenatal sex steroids in the development of digit ratio. *Proc Natl Acad Sci USA* 108: 16143-16144.
- Byne W (2006) Developmental endocrine influences on gender identity: implications for management of disorders of sex development. *Mt Sinai J Med* 73: 950-959.
- Paus R, Stefan Peker S, Sundberg JP (2008) Biology of Hair and Nails. In: Bologna JL, Jorizzo JL, Rapini RP, *Dermatology*. (2<sup>nd</sup> edn), Mosby Elsevier, Spain, 965-986.
- Robinson SJ, Manning JT (2000) The ratio of 2nd to 4th digit length and male homosexuality. *Evol Hum Behav* 21: 333-345.

11. Manning JT, Scutt D, Wilson J, Lewis-Jones DI (1998) The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentrations of testosterone, luteinizing hormone and oestrogen. *Hum Reprod* 13: 3000-3004.
12. Manning JT, Bundred PE, Newton DJ, Flanagan BF (2003) The second to fourth digit ratio and variation in the androgen receptor gene. *Evol Hum Behav* 24: 399-405.
13. Manning JT, Bundred PE, Flanagan BF (2002) The ratio of 2nd to 4th digit length: A Proxy for transactivation activity of the androgen receptor gene? *Med Hypotheses* 59: 334-336.
14. Bilgiç Ö, Doğdu M, İslamoğlu GK, Altınyazar C (2014) The relationship between the second to fourth digit ratio and acne vulgaris. *J Eur Acad Dermatol Venereol* 28: 1340-1343.
15. Bilgiç Ö, Altınyazar HC, Eryılmaz D, Tuğrul ZA (2016) Are 2D: 4D finger-length ratios an indicator of androgenetic alopecia in males? *An Bras Dermatol* 91: 156-159.
16. Bilgiç Ö, Altınyazar C, Hıra H, Doğdu M (2015) Investigation of the Association of the Second-to-Fourth Digit Ratio with Skin Sebum Levels in Females with Acne Vulgaris. *Am J Clin Dermatol* 16: 559-564.
17. Malas MA, Dogan S, Evcil EH, Desdicioglu K (2006) Fetal development of the hand, digits and digit ratio (2D: 4D). *Early Hum Dev* 82: 469-475.
18. Manning J, Kilduff L, Cook C, Crewther B, Fink B (2014) Digit ratio (2D: 4D): A biomarker for prenatal sex steroids and adult sex steroids in challenge situations. *Front Endocrinol* 5: 90.
19. Hönekopp J, Watson S (2010) Meta-analysis of digit ratio 2D:4D shows greater sex difference in the right hand. *Am J Hum Biol* 22: 619-630.
20. Breedlove SM (2010) Minireview: Organizational hypothesis: Instances of the fingerpost. *Endocrinology* 151: 4116-4122.
21. Berenbaum SA (1999) Effects of early androgens on sex-typed activities and interests in adolescents with congenital adrenal hyperplasia. *Horm Behav* 35: 102-110.
22. Chan JL, Kar S, Vanky E, Morin-Papunen L, Piltonen T, et al. (2017) Racial and ethnic differences in the prevalence of metabolic syndrome and its components of metabolic syndrome in women with polycystic ovary syndrome: a regional cross-sectional study. *Am J Obstet Gynecol* 217: 189.e1-189.e8.
23. Abbott DH, Barnett DK, Bruns CM, Dumesic DA (2005) Androgen excess fetal programming of female reproduction: a developmental etiology for polycystic ovary syndrome? *Hum Reprod Update* 11: 357-374.