Second-to-fourth digital length ratio in male patients with acne vulgaris

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Objective
The aim of this study was to evaluate second and fourth digit length ratio in acne vulgaris male patients compared with controls, and to assess the association of this ratio with the clinical aspects of that disease.

Background
The ratio of second-to-fourth digit length (2D:4D) has been hypothesized to reflect prenatal androgen exposure and an individual's sensitivity to androgens.

Patients and methods
The current study was carried out on 169 male patients with different degrees of acne vulgaris severity selected from the Dermatology Outpatient Clinic, Faculty of Medicine, Menoufia University Hospital, Mansoura Dermatology Hospital, from January 2015 to December 2015, in addition to 63 age and sex-matched healthy volunteers as a control group.

Results
Acne patients' ages ranged from 12 to 26 years with a mean age of 19.87 ± 4.487 years, whereas the age of controls ranged from 13 to 36 years with a mean age of 19.54 ± 3.809 years. The control group comprised 63 male patients. There were nonsignificant differences between patients and controls as regards age. No significant differences were found between right digit 2D:4D, left digit 2D:4D, and total digit 2D:4D ratio in male patients and controls. There was a significant positive correlation between severity of acne lesion and right 2D:4D, but nonsignificant correlations were found as regards left and total 2D:4D. Significant negative correlations were found between right, left, and total 2D:4D ratio and disease duration. However, nonsignificant correlations were found between right, left, or total 2D:4D ratio and age of onset of acne lesion.

Conclusion
In male acne cases this 2D:4D ratio might be a good predictor of acne duration only and to the same extent its severity, but not its development.

Introduction

Acne is currently understood as a chronic inflammatory disease of the pilosebaceous unit, characterized by androgen-induced increased sebum production, follicular hyperkeratinization, inflammation, and altered adaptive immune response. The clinical features of acne include seborrhea (excess grease), noninflammatory lesions (open and closed comedones), inflammatory lesions (papules and pustules), and various degrees of scarring. Nodules and cysts comprise severe nodulocystic acne. The distribution of acne corresponds to the highest density of pilosebaceous units [1].

Grading the severity of acne as mild, moderate, or severe is a useful initial assessment. Mild disease comprises open and closed comedones with sparse inflammatory lesions. In moderate acne, papules and pustules are more numerous. Severe acne comprises extensive lesions, and may include nodules and scarring [2].

The presence of higher androgen levels is important for the development of acne lesions. However, the majority of acne patients exhibit normal levels of circulating androgens, suggesting that the impact of androgens on the development of acne lesions might be related to end-organ sensitivity [3,4].

The ratio of second-to-fourth digit length (2D:4D) has been hypothesized to reflect prenatal androgen exposure and an individual's sensitivity to androgens [5].

In general, men have a longer fourth digit (ring finger) relative to the second digit (index finger) compared with women, and many studies have supported this sexually dimorphic feature [6].

Exposure to higher androgen levels through the prenatal period is related to a lower 2D:4D ratio in both sexes. For instance, lower 2D:4D (male type) digit ratios were found in both female and male populations with congenital adrenal hyperplasia compared with healthy sex-matched controls [7,8].

Higher (female type) digit ratios are also found in XY male patients with androgen insensitivity syndrome, and this may be an indicator of their importance in end-organ sensitivity [9,10].

Prenatal androgen levels increase at the end of the first trimester and affect a number of organ systems [5,6]. Dressler and Voracek [11] have evaluated the impact of prenatal androgens on some physical, psychological, and medical conditions, such as aggression, athletic performance, autism, fertility, many cancers, and heart diseases, using the 2D:4D ratio.

The prenatal androgen peak time period (between 13 and 15 weeks of gestation) coincides with the development of both the sebaceous gland and the digits [12].

The aim of this study was to evaluate second and fourth digit length ratio (2D:4D) in male acne vulgaris patients and to assess the association of this ratio with the clinical aspects (duration and or severity) of that disease.

Patients and methods

This case–control study included 169 male patients with different degrees of acne vulgaris severity. In addition, the adequate age-matched healthy volunteers served as controls.

Written consent was obtained from every participant included in this study. The protocol was approved from the Ethical Committee, Faculty of Medicine, Menoufia University.

Inclusion criteria were as follows: male sex and age of at least 16 years to exclude possible effects of puberty.

Exclusion criteria were as follows: a history of injury or illness that leads to deformities on the hands or fingers and a history of drugs that may induce acne.

Methods
(1) Thorough history taking, including personal history, present and past history, and family history
(2) General examination to exclude any systemic disease that may affect hands or finger length

(3) Dermatological examination to assure acne diagnosis and evaluate the degree of its severity
   (a) Mild acne, the presence of comedones as well as few-to-several papules and pustules
   (b) Moderate acne, distinguished by several papules, pustules, and few-to-several nodules
   (c) Severe acne, characterized by numerous or extensive papules and pustules, or both, along with many nodules
   (d) Very severe forms of acne, including the most destructive conditions of the disease, such as acne conglobata, acne fulminans, and the follicular occlusion triad
(4) Finger measurements using digital vernier caliper and 2D:4D ratio were obtained by dividing the length of the index finger by the length of middle finger (Fig. 1) [13].

Statistical analysis
The data collected were tabulated and analyzed using SPSS (statistical package for the social science software) statistical package, version 20 (version 20; SPSS Inc., Chicago, Illinois, USA) on IBM compatible computer.

Two types of statistics were carried out: descriptive statistics and analytic statistics

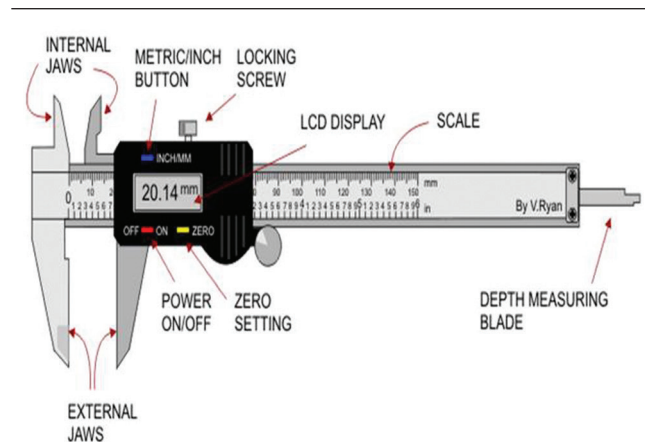### Descriptive statistics
Descriptive statistics were expressed as mean ± SD and median and range for quantitative data or number and percentage for qualitative data.

Analytic statistics
(1) χ^2: It is the test of significance used to study the association between two qualitative variables

Figure 1

The digital vernier caliper with a resolution of 0.01 mm.

(2) Student's *t*-test: It is a test of significance used for comparison between two groups of normally distributed quantitative variables

(3) Mann–Whitney test (nonparametric test): It is a test of significance used for comparison between two groups of non-normally distributed quantitative variables

(4) Correlation was used for quantitative variables that were not normally distributed or when one of the variables is qualitative.

A *P*-value at 0.05 was used to determine significance as follows:

A *P*-value more than 0.05 to be statistically nonsignificant.

A *P*-value of up to 0.05 to be statistically significant.

A *P*-value of up to 0.001 to be highly statistically significant.

Results

This case–control study was carried out on 232 participants; 169 acne vulgaris cases and 63 age and sex-matched healthy individuals as a control group. In the acne group, the age of male patients (169 patients) showed a median value of 18 years, which ranged from 13 to 38 years with a mean ± SD value of 18.52 ± 2.99 (Table 1).

No significant difference between the studied cases and controls could be detected as regards their age (*P* = 0.329) (Table 2).

Right (2D:4D) ratio in controls ranged from 0.9024 to 1.05488 with 0.966682 as median value and 0.971 ± 0.029 as mean ± SD. Among male patients with acne vulgaris, right (2D:4D) ratio ranged from 0.8472 to 1.22801 with 0.96963 as a median value and its mean ± SD was 0.966 ± 0.037. There was no significant difference between right (2D:4D) ratio mean value in male patients and controls (*P* = 0.398) (Table 3).

Compared with controls, left (2D:4D) ratio in male patients with acne vulgaris was nonsignificantly (*P* = 0.905) elevated (0.968 ± 0.029 and 0.968 ± 0.031, respectively) (Table 4).

No significant difference (*P* = 0.834) was found in total digit ratio between male patients (0.967 ± 0.027) and controls (0.969 ± 0.028) (Table 5).

In the right hand, there was a significant positive correlation between calculated right (2D:4D) ratio and acne vulgaris severity (*P* = 0.038, *r* = 0.159) (Fig. 2).

Table 1 Demographic data of studied participants

Variables	Controls (N=63)	Male cases (N=169)
n (%)	63 (27.3)	169 (32.4)
Age (years)		
Mean±SD	18.63±3.189	18.52±2.991
Median	18	18
Range	14-27	13-28

Table 2 Comparison between cases and controls as regards their age

Variables	The studied groups		*P*
	Controls (N=169)	Cases (N=63)	
Age (mean±SD) (years)	18.52±2.991	18.63±3.189	0.329
Median	18	18	
Range	13-28	14-27	

Table 3 Comparison between right digit ratio in male patients and matched controls

Variables	Control	Cases	*P*
Right			
Mean±SD	0.971±0.029	0.966±0.037	0.398
Median	0.966682	0.96963	
Range	0.9024-1.05488	0.8472-1.22801	

Table 4 Comparison between left digit ratio in male patients and matched controls

Variables	Control	Cases	*P*
Left			
Mean±SD	0.968±0.029	0.968±0.031	0.905
Median	0.972125	0.97051	
Range	0.90069-1.0440	0.87517-1.1706	

Table 5 Comparison between total digit ratio in male patients and matched controls

Variables	Control	Cases	*P*
Total			
Mean±SD	0.969±0.028	0.967±0.027	0.834
Median	0.9684	0.9667	
Range	0.92-1.04	0.88-1.08	

In addition, a significant negative correlation was found between right (2D:4D) ratio in male patients and duration of acne vulgaris (*P* = 0.009, *r* = –0.201) (Fig. 3).

As regards estimated left (2D:4D) ratio in male acne patients, there was a significant negative correlation between left (2D:4D) ratio and disease duration (*P* = 0.015, *r* = –0.187) (Fig. 4).

Concerning total (2D:4D) ratio result in male patients with acne, there was a significant negative correlation between total (2D:4D) ratio and the disease duration (*P* = 0.010, *r* = 0.198) (Fig. 5).
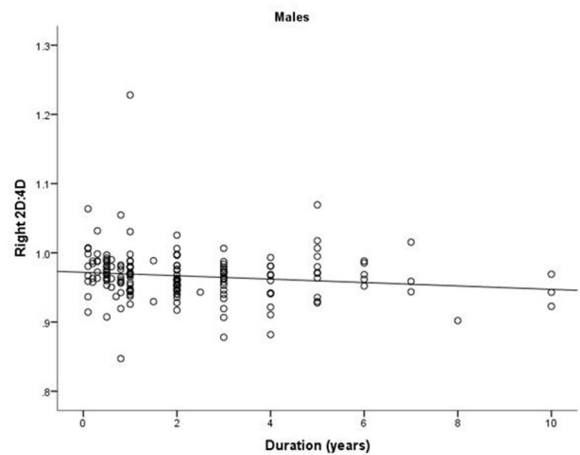
Discussion

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit that has increased in frequency
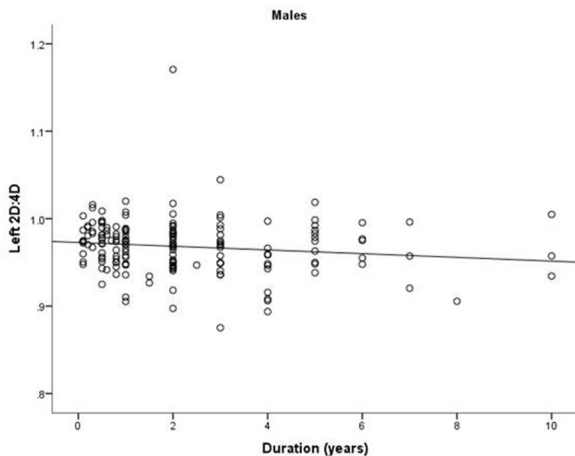
Figure 2
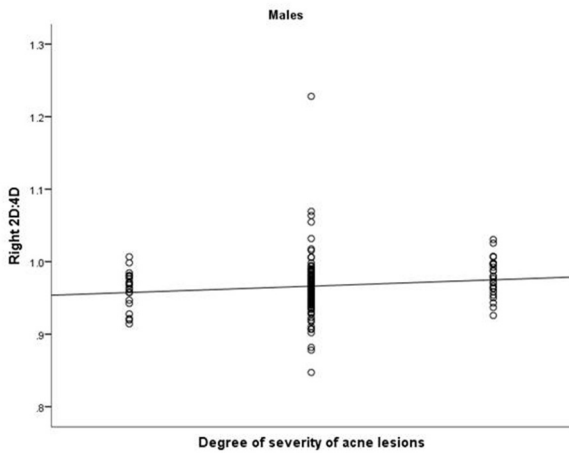
Correlation of right 2D:4D ratio with degree of acne severity in male patients. 2D:4D, second and fourth digit length ratio.
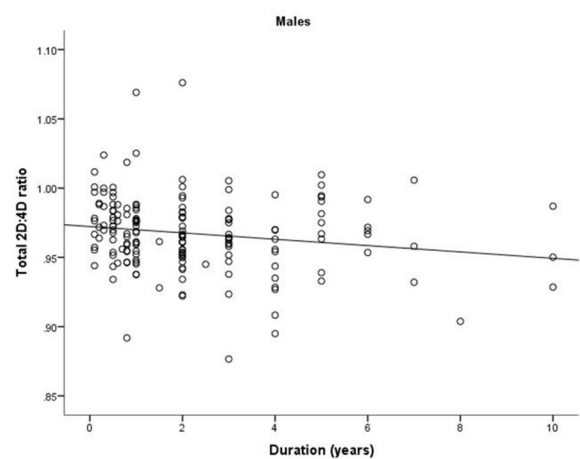
Figure 3

Correlation of right 2D:4D ratio with disease duration in male patients. 2D:4D, second and fourth digit length ratio.

Figure 4

Correlation of left 2D:4D ratio with disease duration in male patients. 2D:4D, second and fourth digit length ratio.

Figure 5

Correlation of total 2D:4D with disease duration in male patients. 2D:4D, second and fourth digit length ratio.

in the last half century. The disease is characterized by hormonally mediated sebum overproduction, follicular hyperkeratinization, and an increased release of inflammatory mediators. Androgen hormones are thought to increase sebum secretion, giving rise to increased keratinization of the follicular infundibulum and leading to microcomedone formation [14].

Taylor *et al.* [14] have shown that boys who are castrated before the onset of puberty do not develop acne vulgaris (AV). Similarly, post-adolescent castration or oophorectomy in patients with AV results in the gradual resolution of acne lesions. The presence of androgen is important for the development of acne lesions. Moreover, men with complete androgen insensitivity had no detectable sebum excretion and no acne development.

The 2D:4D digit ratio refers to the ratio of the length of the second finger (index finger) to that of the fourth

finger (ring finger). Three possible relationships of relative finger length may occur: index finger shorter than ring finger ($2^{nd} < 4^{th}$), index finger equal in length to ring finger ($2^{nd} = 4^{th}$), or index finger longer than ring finger ($2^{nd} > 4^{th}$). In recent years, the 2D:4D ratio has attracted more attention, when it was recognized that a longer index finger relative to the ring finger is found more frequently in women than in men. The balance between fetal testosterone and fetal estrogen during the prenatal period largely determines this ratio, which does not change with age in the postnatal period [15].

Prenatal androgen levels increase at the end of the first trimester and affect a number of organ systems. The prenatal androgen peak time period (between 13 and 15 weeks of gestation) coincides with both the development of the sebaceous gland and digits. Thus, there is an association between finger length and acne development [16].

Deficient research studies in that field encourage us to study this issue for more explanation of the role of 2D:4D ratio acne vulgaris development and evaluation.

In this study, we aimed to assess 2D:4D ratio in male acne vulgaris patients compared with controls, and to investigate the association of this ratio with the clinical aspects (duration, severity, and age of onset) of that disease.

In this study, the age of acne vulgaris patients ranged from 12 to 26 years with a mean age of 19.87 ± 4.487. In agreement with that, Saitta *et al.* [17] reported that acne vulgaris can affect people of all age groups, but it is most prevalent in adolescence. Over 90% of male and 80% of female populations have experienced acne by the age of 21.

Concerning acne severity, most of our patients (66%) presented with moderate acne and the minority of patients (12.3%) presented with mild form, whereas the incidence of the severe form was lowest (13%). Moreover, Bilgic *et al.* [18] reported that the majority of patients had moderate acne (61%), followed by severe acne (31.1%), and mild acne was observed only in 8%.

In our study, there were no significant differences ($P < 0.05$) found between male acne patients and their matched controls as regards their right digit 2D:4D ratio (0.966 ± 0.03 vs. 0.971 ± 0.029), left digit 2D:4D ratio (0.968 ± 0.03 vs. 0.968 ± 0.029), and total digit 2D:4D ratio (0.967 ± 0.027 vs. 0.969 ± 0.028).

This is in agreement with the findings of Bilgic *et al.* [18], who did not find any significant differences between male patients with AV and the control group, as we reported. However, Unal *et al.* [19] reported no statistically significant difference between male acne patients and their matched controls as regards the 2D:4D ratio for the right and the left hand (separately) or for the average (total) 2D:4D ratio of both hands.

In the present work, on studying the association between 2D:4D ratio and clinical data of male acne cases, the result revealed significant negative correlations between right ($P = 0.009$, $r = -0.201$), left ($P = 0.015$, $r = -0.187$), and total ($P = 0.010$, $r = -0.198$) 2D:4D ratio with disease duration. There was a significant positive correlation between right (2D:4D) ratio and acne severity ($P = 0.038$, $r = 0.159$).

As regards acne severity in male patients, there were no significant correlations between left ($P = 0.219$, $r = 0.004$) or total ($P = 0.224$, $r = 0.003$) 2D:4D and this severity. This finding supports the result of Manning *et al.* [15], who suggested that right (2D:4D) ratio is more sensitive to prenatal androgen compared with the left. Thus, we can conclude that, in male acne patients, although the lower 2D:4D ratios (more masculine) were nonsignificant compared with controls, these ratios have a negative impact on acne duration. Moreover, the low right (2D:4D) ratio has a delirious effect on acne severity.

However, Unal *et al.* [19] in their study on 52 male Turkish acne patients detected no correlations between the 2D:4D ratios for the right and left hands separately or total 2D:4D ratio of both hands and age of onset, disease duration, or disease severity.

This suggests that androgen exposure is only a susceptibility factor for triggering on initiating acne development. Moreover, as acne is a multifactorial disease, factors other than androgens may be responsible for acne severity.

As regards age of onset of acne vulgaris in our cases, no associations were detected between right (2D:4D) ratio ($P = 0.611$), left (2D:4D) ratio ($P = 0.341$), or total (2D:4D) ratio ($P = 0.375$) with age of acne onset. This is in line with the results of Unal *et al.* [19], who found no association between right, left, or total 2D:4D ratios and onset of acne lesions in their study in male acne patients.

Conclusion
On the basis of the result of this study and its discussion, it could be concluded that 2D:4D ratio might be a good predictor of acne duration only and to the same extent its severity, but not its development.

Conflicts of interest
There are no conflicts of interest.

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