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Original Article

Serum levels of testosterone and dehydroepiandrosterone sulfate in females with acne and/or female pattern hair loss

Raman Balakrishna Venkatta[1], Sheena Ann Simon[2], K. Abdul Samad[3], Anuja Elizabeth George[2]

[1]Department of Health Services, Palakkad, [2]Department of Dermatology and Venereology, Government Medical College, Thiruvananthapuram, [3]Department of Dermatology, Government Medical College, Kozhikode, Kerala, India.

***Corresponding author:**
Raman Balakrishna Venkatta, Department of Health Services, Palakkad, Kerala, India.

doctor82@gmail.com

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ABSTRACT

Objectives: The objectives of this study are as follows: (1) To study the levels of testosterone and dehydroepiandrosterone sulfate (DHEAS) in females with acne and/or female pattern hair loss (FPHL) and (2) to study the correlation of the severity of acne and/or FPHL with serum levels of testosterone and DHEAS.

Materials and Methods: A cross-sectional study was carried out in the department of dermatology and venereology, of a tertiary care institution over a period of 1 year among patients who presented with acne and/or FPHL. Acne was graded using Leeds revised acne grading system and FPHL with Ludwig scale. Competitive immunoenzymatic colorimetric method for quantitative determination of testosterone and DHEAS concentrations in serum ("DiaMetra" kits) was performed. Correlation between quantitative variables was assessed by Pearson correlation and Spearman rank correlation.

Results: A total of 84 patients with acne and/FPHL were studied over a period of 1 year. Fifty-one (60.7%) patients had acne, 21 (25%) had FPHL, and 12 (14.3%) patients had both. The mean levels of testosterone in acne, FPHL, and in patients with both were 1.14 ± 4.65 ng/ml, 0.51 ± 0.17 ng/ml, and 0.53 ± 0.24 ng/ml, respectively. The mean DHEAS in patients with acne, FPHL, and with both was 4.64 ± 4.96 μg/ml, 4.96 ± 5.34 μg/ml, and 6.34 ± 5.37 μg/ml, respectively. The Spearman rank correlation between the level of testosterone and the grades of inflammatory acne in face and FPHL was 0.193 and -0.16, respectively. The Spearman rank correlation of DHEAS with the grades of inflammatory acne in face and FPHL was 0.092 and 0.01, respectively.

Limitations: The study carried out in a tertiary referral center, not reflecting the status of the condition in general population was the major limitation.

Conclusion: This study in a localized population could not elicit a significant statistical correlation between serum levels of total testosterone and DHEAS with severity of acne or FPHL. However, a majority of patients with acne, FPHL, or both had low levels of total testosterone which were discordant with most of the previous studies. Half of the study population with coexisting acne and FPHL had high levels of DHEAS which suggests the need to study the role of DHES in patients with coexistence of acne and FPHL.

Keywords: Acne, Pattern hair loss, Female pattern hair loss, Testosterone, Dehydroepiandrosterone sulfate

INTRODUCTION

Acne vulgaris is the most common dermatologic disorder and has a lifetime prevalence of 70%-90%.[1] About 10% of pre-menopausal women develop female pattern hair loss (FPHL), which increase to 20%–30% in postmenopausal women.[2] Thus, both these conditions affect one's

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appearance and cause considerable psychosocial distress in the affected women in their most productive years of lives.

Even though acne is principally a disorder of adolescence, the prevalence of acne in adults is increasing.[3] Both these disorders are determined by androgens and potential of the pilosebaceous unit to respond to the hormonal changes. Adult acne cases account for 25% of the total acne population. More than one-third of women with adult acne have additional clinical features of hyperandrogenicity.[4]

Testosterone and dehydroepiandrosterone sulfate (DHEAS) are the two principal androgens that are incriminated in previous studies in the pathogenesis of acne and FPHL.[5,6] Hyperandrogenic conditions can be treated effectively by various hormonal and therapeutic interventions. However, a hyperandrogenic state has not yet been consistently observed in all the previous studies. Furthermore, no studies on the levels of testosterone and DHEAS in females in our population could be found after searching the available literature.

Hence, this study focuses on the levels of testosterone and DHEAS in females with the two androgen-related disorders: Acne and FPHL.

MATERIALS AND METHODS

This cross-sectional study was conducted in the dermatology department of a tertiary care center.

Schiavone *et al*. studied 24 women with acne and studied the levels of testosterone and DHEAS.[5] Skalnaya and Tkachev studied 153 women with FPHL and determined the levels of testosterone and DHEAS.[6] The above studies were used to determine the sample size and the following formula was used.

{Formula: N= (Z1-α/2)2σ2/d2, N = Sample size, σ = standard deviation (SD), d = Precision)

The desired level of precision was set at 10% of the mean. Value of sample size for both testosterone and DHEAS was calculated and the higher value of the two was chosen for acne and FPHL, respectively.

Acne: N = 63 (SD = 24, Mean = 59.24); FPHL: N=19 (SD = 0.64, Mean = 2.86)}

Consecutive female patients of any age presenting to the outpatient clinic of our department with acne and/or FPHL for a period of 1 year from 28/11/2015 were included in the study.

Patients with acne and/or patterned hair loss who were not consenting for the study, patients on steroids/hormonal supplements/oral contraceptive pills and pregnant females were excluded from the study.

Informed written consent was obtained from parent/guardian in case of a patient less than 18 years of age. An assent from the patient was obtained between the ages of 12 and 18. Informed written consent was obtained from patients more than 18 years of age. Institutional ethics committee approved the study.

FPHL was diagnosed when a female presented with a generalized reduction in density of hair over the crown and frontal scalp with preservation of the frontal hairline with or without complaints of increased shedding of hair.[7]

A preset pro forma was used to record the data. Demographic data, detailed history pertaining to the lesion, and of any associated illnesses were collected. Clinical findings were interpreted with the help of Leeds revised acne grading system (LRAGS) in case of acne.[8] Ludwig scale was used to interpret the clinical findings in case of FPHL.[9] Complete hemogram and thyroid function test were done in all participants. Competitive immunoenzymatic colorimetric method (DiaMetra kits) was used for quantitative determination of total testosterone and DHEAS in serum. The reference range for testosterone was taken as 0.2–1.2 ng/ml and that for DHEAS was taken as 0.9–3.6 μg/ml as mentioned in the test kits.

Data were entered into Microsoft Excel. Statistical analysis was performed using trial version of SPSS software. Quantitative variables were expressed as mean and SD. Qualitative variables were expressed as frequency and percentage. Correlation between quantitative variables was assessed by Pearson correlation and Spearman rank correlation. $P < 0.05$ was considered as statistically significant.

RESULTS

During the 1 year period, a total of 84 women with acne and/or FPHL were examined. Fifty-one patients (60.7%) had acne alone, 21 patients (25%) had FPHL alone, and 12 patients (14.3%) had both acne and FPHL. Forty patients with acne were less than 30 years of age (78.4%). Among FPHL patients, ten were below 30 years (47.6%). Among patients with both acne and FPHL, ten patients (83.3%) were less than 30 years. Among patients with acne, the age ranged from 11 years to 46 years (mean – 24.1 ± 7.7). The age ranged from 11 years to 60 years (mean – 31.9 ± 12.9) in the FPHL group. The age ranged from 11 to 38 years (mean – 24 ± 8.6 years) in patients with both acne and FPHL.

Thirty-five patients (68.6%) with acne and seven patients with both acne and FPHL (58.3%) were students. Seventeen patients with FPHL were housewives (81%).

Thirty-five patients (68.6%) with acne were unmarried. Eighteen patients with FPHL (85.7%) and six patients with both acne and FPHL (50%) were married.

There was history of thyroid disorders in seven patients out of the total 84 patients (8.3%). Majority of the patients had no history of other illnesses (59, 70.2%). One patient with acne gave history of polycystic ovarian disease [Table 1].

Six patients with acne (11.8%), seven patients with FPHL (33.3%), and three patients with both acne and FPHL (25%) had menstrual abnormalities.

Two patients (2/51, 3.9%) with acne had history of treatment for hirsutism. None of the patients with FPHL had hirsutism. None of the patients with acne, FPHL, or both had acanthosis nigricans.

Sixty-three patients (75% of total 84 patients) had no family history of either acne or FPHL. Ten patients (19.6%) with acne and two patients with both acne and FPHL (16.7%) had family history of acne. Seven patients with FPHL (33.3%) and two patients with both acne and FPHL (16. 7%) had family history suggestive of FPHL.

Twenty-eight patients with acne (54.9%), eight patients with FPHL (38.1%), and eight patients with both acne and FPHL (66.7%) had normal body mass index (BMI). Sixteen patients with acne (31.4%), 11 patients with FPHL (52.4%), and two patients with both acne and FPHL (16.7%) were either overweight or obese. Seven patients with acne (13.7%), two patients with FPHL (9.5%), and two patients with both acne and FPHL (16.7%) had low BMI.

Table 1: Associated diseases in study participants with acne and/or female pattern hair loss.

Associated disease	Number of patients (% of total) *n*=84
None	59 (70.2)
Thyroid disorder	7 (8.3)
Atopy	4 (4.8)
Eczemas	4 (4.8)
Psychiatric disorders	3 (3.6)
Dermatophytosis	2 (2.4)
Chronic urticarial	2 (2.4)
Polycystic ovarian disease	1 (1.2)
Others	6 (7.1)

All the 63 patients with acne lesions (51 with acne alone and 12 with acne and FPHL) had lesions affecting the face. All the 63 cases had inflammatory facial acne. None of the patients had purely comedonal acne. Acne involved the chest in 23/63 cases (36.5%) and 34 patients (54%) had involvement of back.

Forty-nine (77.8%) of 63 patients with facial acne had LRAGS score of 4 to 8 and, thus, had moderate-to-severe grades of inflammatory acne. Acne involving the chest was of LRAGS score three and below (mild acne) in 20/23 (87%) cases. Acne affecting the back was of LRAGS score three and below in 32/34 cases (94.1%).

Among the total 33 patients with FPHL (21 with FPHL alone and 12 with FPHL and acne), 19 (57.6%) had Ludwig Grade I and 14 patients (42.4%) had Ludwig grade II severity. There were no patients with Grade 3 severity.

All the study participants had normal LFT and RFT.

One patient each with acne (1/51, 2%) FPHL (1/21, 4.8%) and with both acne FPHL (1/12, 8.3%) had elevated T3 levels. One patient each with acne, FPHL, and both conditions (1.9%, 4.8%, and 8.3%, respectively) were having low T4 levels. Two patients with acne (2/21, 3.9%) and two patients with FPHL (2/51, 9.5%) were having high T4 levels. One patient with FPHL (4.8%) and one patient (8.3%) with both acne and FPHL had low thyroid stimulating hormone levels.

The mean levels of testosterone in patients manifesting acne, FPHL, and in patients with both were 1.14 ± 4.65 ng/ml, 0.51 ± 0.17 ng/ml, and 0.53 ± 0.24 ng/ml, respectively. Testosterone ranged from 0.002–35.300, 0.003–3.25, and 0.02–2.7 ng/ml, respectively, in patients with acne, FPHL, and both [Table 2].

The mean DHEAS levels in patients with acne, FPHL, and with both were 4.64 ± 4.96 µg/ml, 4.96 ± 5.34 µg/ml, and 6.34 ± 5.37

Table 2: Serum testosterone and dehydroepiandrosterone sulfate levels in female patients with acne and/or female pattern hair loss.

Study participants	Hormone level					
	Testosterone (ng/ml)			Dehydroepiandrosterone sulfate (µg/ml)		
	Low	Normal	High	Low	Normal	High
Patients with acne alone	27	19	5	9	23	19
n=51	52.9%	37.3%	9.8%	17.6%	45.1%	37.3%
Patients with female pattern hair loss alone	12	7	2	9	7	5
n=21	57.1%	33.3%	9.5%	42.9%	33.3%	23.8%
Patients with acne and female pattern hair loss	6	4	2	2	4	6
n=12	50%	33.3%	16.7%	16.7%	33.3%	50%
Total	45	30	9	20	34	30
N=84	53.6%	35.7%	10.7%	23.8%	40.5%	35.7%

μg/ml, respectively. DHEAS ranged from 0.22–22.1 μg/ml, 0.26–18.1 μg/ml, and 0.79–16.24 μg/ml, respectively, in patients with acne, FPHL, and with both, respectively [Table 2].

The Spearman rank correlation between testosterone levels and DHEAS level was 0.173 [Table 3]. The Spearman rank correlation between the level of testosterone and the grades of inflammatory acne in face was 0.193. The Spearman rank correlation between the level of testosterone and the grades of acne in back and chest was 0.124 and 0.093, respectively. The Spearman rank correlation between the levels of testosterone and the grades of FPHL was –0.160.

The Spearman rank correlation of DHEAS with the grades of inflammatory acne and non-inflammatory acne in face was 0.092 and 0.023, respectively [Table 4]. The Spearman rank correlation of DHEAS with grades of acne in back and chest was 0.141 and 0.168, respectively. The Spearman rank correlation of DHEAS with the grades of FPHL was 0.010.

DISCUSSION

The age of patients with acne (24.1 ± 7.7) documented by us was consistent with previous data.[10] The mean age of those affected with FPHL as noted by us (31.9 ± 12.9) was comparable to literature (29.9 ± 9.6 years).[11] The mean age of those with coexisting acne and FPHL (23.2 ± 4.1) was also concordant to literature (24.4 ± 6.4).[12]

Table 3: Correlation of serum testosterone levels with level of dehydroepiandrosterone sulfate and acne and/or female pattern hair loss.

Parameters assessed	Spearman rank correlation	*P*-value
Serum dehydroepiandrosterone sulfate	0.173	0.115
Acne lesions face (LRAGS)	0.193	0.079
Acne lesions back (LRAGS)	0.124	0.262
Acne lesions chest (LRAGS)	0.093	0.398
Ludwig grade of female pattern hair loss	–0.160	0.145

LRAGS: Leeds revised acne grading system

Table 4: Correlation of serum dehydroepiandrosterone sulfate level with acne and/or female pattern hair loss.

Parameters assessed	Spearman rank correlation	*P*-value
Acne lesions face (LRAGS)	0.092	0.405
Acne lesions back (LRAGS)	0.141	0.202
Acne lesions chest (LRAGS)	0.168	0.127
Ludwig grade of female pattern hair loss	0.010	0.929

LRAGS: Leeds revised acne grading system

Fifty patients among the total patients with acne (50/63, 79.4%) and 20 patients (20/33, 60.6%) among the total patients with FPHL were less than 30 years. We categorized patients into those aged 30 years and above and those below 30 years since previous authors noted that about 12% of women develop clinically detectable FPHL by the age of 29 years.[13,14] A cutoff of 30 years has been used by others while categorizing FPHL patients.[11] We observed FPHL in young and old, whereas acne manifested predominantly in younger age group.

In this study, seven patients (5.9%) were having thyroid disorders which were comparable to the findings of Okram *et al*., but lower than the same noted in certain other studies.[11,15] Our observations of family history of acne in 19.6% of patients with acne and in 16.7% of patients with both acne and FPHL were lower than the observations of others.[3,11] Okram *et al*. noted that 38% of patients with FPHL had a family history of hair loss, which was comparable to our findings.[11]

In the study by Lawrence *et al*., 48.9% of patients with acne had menstrual abnormalities, which were higher than the 14.3% observed by us (nine out of the 63 patients who had acne with or without FPHL).[16]

The mean BMI observed among patients who had acne, FPHL, and both by us was comparable to literature.[12]

One out of the nine patients with elevated testosterone (11.1%) and 5 out of the 30 patients (16.7%) with elevated DHEAS had menstrual abnormalities. This was lower than the same reported (38.4%) earlier.[12]

None of the patients in this study showed purely comedonal acne. In a large study by Tan *et al*., purely comedonal acne was seen in only 6% of total acne patients.[17] Sixty-one patients (96.8%) in this study had accompanying non-inflammatory acne. This was higher than the 34.1% observed by Guerra-Tapia *et al*.[1]

Only 22.2% of patients manifesting inflammatory facial acne of LRAGS grade four or less was lower than the 33.3% noted by Guerra-Tapia *et al*. and 69.9% observed by Tan *et al*.[1,17]

More than 80% of patients with acne over the chest having a LRAGS score of 3 or less noted by us was higher than the observations of Guerra-Tapia *et al*. (48.7%) and Tan *et al*. (65.6%).[1,17]

The same studies noted that 56.4% (Guerra-Tapia *et al*.) and 68.3% (Tan *et al*.) of patients with acne over back had a LRAGS score of 3 or less 0. This was lower than the 94% noted by us (32/34).[1,17]

The distribution of FPHL into different grades as per Ludwig classification noted by us (57.6% showing Ludwig Grade I and 42.4% showing Ludwig Grade II severity) was concordant to literature.[18]

The mean testosterone level of the patients with acne noted by us (1.14 ng/ml) was higher than the previous reports (0.46–0.59 ng/ml).[5,12] But we found normal or low level of serum testosterone in 56 (88.9%) out of the 63 study participants with acne. The higher mean value for serum testosterone noted by us was due to the very high values of the same observed in a few study participants with acne.

The testosterone levels in those with FPHL documented by us were 0.51 ng/ml, which were consistent with previous studies.[6]

Increased 5α-reductase activity and increased levels of dihydrotestosterone, which are formed by the peripheral conversion of testosterone by 5α-reductase, are thought to be a pathogenetic factor in both acne and FPHL.[19] Whether the low values of testosterone observed in most of the patients with acne and/or FPHL are a reflection of the increased peripheral conversion of testosterone to dihydrotestosterone needs analysis in future studies.

Free testosterone, which is the major determinant of the hormonal action in peripheral tissues, constitutes only about 2% of total testosterone.[20] The alterations in ratios of the levels of total testosterone, free testosterone, 5α-reductase, and sex hormone binding globulin need to be studied in patients with acne and/or FPHL.

The mean level of DHEAS in patients with acne (4.64 μg/ml) was higher than the same observed by others (2.1–2.73 μg/ml).[5,12]

The mean DHEAS in patients with FPHL observed by us (4.96 ± μg/ml) was higher than the same found earlier (1–2.1 μg/ml).[6,12] We noted a higher mean DHEAS in patients with both acne and FPHL (6.34 μg/ml) when compared to previous studies (2.3 μg/ml).[12]

We found that the testosterone levels were low or normal in most of the patients with acne, FPHL, or both. Most of the patients with isolated FPHL or acne had low or normal levels of DHEAS, whereas 50% of patients with both acne and FPHL had DHES above the upper limit of the normal.

No significant correlation was observed between the levels of testosterone and DHEAS. No correlation was noted between the severity of acne or FPHL and the levels of testosterone or DHEAS. All the values obtained were closer to zero which indicated a weak association between the ranks.

Limitations

The study conducted in a referral center not reflecting the status of the disease in the population was the major limitation.

CONCLUSION

This study in a population of 84 patients attending a tertiary referral center could not elicit a significant statistical correlation between serum levels of total testosterone and DHEAS with severity of acne or FPHL. However, a majority of patients with acne, FPHL, or both were found to have low levels of total testosterone which are discordant to most of the previous studies. Half of the study population with coexisting acne and FPHL had high levels of DHEAS which suggests that the significance DHEAS levels in women with coexisting acne and FPHL needs assessment in future studies with large sample size.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

Dr. K. Abdul Samad and Dr. Anuja Elizabeth George are on the editorial board of the Journal.

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