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Evaluation of Trigger Factors and Hormonal Abnormalities in Adult Female Acne

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ABSTRACT
Women's acne, which can start in youth and last into age, is frequently linked to anxiety and sadness. Its etiopathogenesis is influenced by genetic and hormonal variables and because of the clinical progression, maintenance therapy is necessary, typically for years. Recurrent acne, a third form of acne that has lately been proposed in addition to chronic and late acne and that first appears in adolescence, improves for an undetermined amount of time and then reappears in maturity. There aren't many papers on this since modern research seldom asks the patient if acne returned after an adolescent era, while querying the age of acne start. Nonpregnant females with acne aged 25 years who had not been on hormone medication for the previous three months were the subjects of this prospective research conducted at the RVM Medical College's Department of Dermatology's Outpatient Clinic. A thorough history was obtained and a proforma that had been authorized in advance was followed. A pre-designed proforma was used to examine patients with acne under the age of 25 in order to identify trigger factors and rate the severity of the acne using the Global Acne Grading System (GAGS). Total testosterone (TT), AMH, 17-hydroxyprogesterone (17-OHP), dehydroepiandrosterone sulfate (DHEAS), sex hormone binding globulin (SHBG), free androgen index (FAI), follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH) and prolactin were all measured as part of a thorough hormonal evaluation. Just 4.28% of acne patients were beyond the age of 40, while the majority of acne patients (58.57%) were between the ages of 21 and 30. About 70 adult female acne patients were seen and 61.42% of the women had late-onset acne, whereas 38.57% had chronic acne. Papules were the most prevalent lesion at the time of presentation (61.42%), followed by mixed lesions, which included pustules and nodules. The severity of the patient's acne was rated as mild (72.8%), moderate (25.71%), or severe (1.42%). According to the subjective assessment, 21.3% of women experienced a clear premenstrual flare. The objective evaluation found that nutrition had a role in the health of 23.33% of patients, with "oily" and dairy products being prevalent items, sugar products and cosmetics, fairness creams, foundations, facials and change of life style, with lack of physical excessive, obesity. Fairness creams, foundations and facials were among the cosmetics that were at fault. While sunscreens had the highest maximum frequency per month, "fairness creams" were found to have the highest mean duration. Diet, stress and cosmetics may all contribute to adult female acne and a specific hormonal environment is responsible for both hyperandrogenemia and elevated levels of adrenal androgen. We discovered that stress and sleep deprivation were both prevalent in a significant number of individuals with high levels of adrenal hormones, suggesting a shaky connection between stress and acne. We have also established that adult female acne patients had elevated AMH levels and more research on this hormone in adult acne patients is needed.

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Key Words
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INTRODUCTION

Diet, stress and cosmetics may all contribute to adult female acne and a specific hormonal environment is responsible for both hyperandrogenemia and elevated levels of adrenal androgen. We discovered that stress and sleep deprivation were both prevalent in a significant number of individuals with high levels of adrenal hormones, suggesting a shaky connection between stress and acne. We have also established that adult female acne patients had elevated AMH levels and more research on this hormone in adult acne patients is needed.

An rising number of adult females are affected by acne, which lowers quality of life and has severe psychological effects as well as social repercussions[1]. Adult female acne (AFA) is a condition that affects women over the age of 25 and may develop for the first time during this time or continue intermittently from youth[2]. Genetic and hormonal variables are thought to have a role in the pathophysiology of AFA, which is characterized by chronic evolution and requires maintenance therapy, often for years[3].

A 1979 article revealed that 5% of ladies between the ages of 40 and 49.5 still had acne, which was rather frequent in individuals over 18 years old. Acne in people over 25 years old didn't start receiving greater attention until 1997, when statistics revealed that 76% of these patients were women, with a mean age of 35.5 years[4]. Only 18.4% of females experienced late acne, which started after 25 years and was mostly brought on by changes in hyperandrogenism and chronic acne accounted for the majority of instances. Other research have verified that chronic acne is more prevalent than acne that first appears as an adult[5].

According to some experts, adult females are more likely to develop acne than adult males in all age categories and acne can linger even after 50. Recurrent acne, a third form of acne that has lately been proposed in addition to chronic and late acne and that first appears in adolescence, improves for an undetermined amount of time and then reappears in maturity[6]. There aren't many papers on this since modern research seldom asks the patient if acne returned after an adolescent era, while querying the age of acne start[7]. Some writers categorize AFA into two groups: Those between the ages of 25 and 44 and those over 45 who are approaching menopause, however the specifics of each category still need to be properly characterized[8].

MATERIALS AND METHODS

In this prospective study, females with acne who were not pregnant and older than 25 and who had not been receiving hormone treatment for the previous three months were assessed in the dermatology department's outpatient clinic. A thorough history was obtained and a proforma that had been authorized in advance was followed. The acne was graded using the Global Acne Grading System (GAGS). Persistent and late-onset acne were separated in the individuals.

Subjective triggers were defined as the elements the patient described causing an acne flare, whereas objective trigger evaluation was reached by asking precise questions on diet, cosmetics, stress and sleep patterns. Dietary history was evaluated using the glycemic index of foods and consumption of milk and dairy products, processed foods, chocolates and "oily" foods, dairy products, sugar products and cosmetics such as fairness creams, foundations and facials as well as a change in lifestyle that resulted in obesity and a lack of excessive physical activity was noted. The comedogenicity of cosmetic compounds such cocoa butter, decyl oleate, isopropyl palmitate, isopropyl myristate, isopropyl isostearate, myristyl myristate butyl stearate and isocetyl stearate was examined[6].

The potential comedogenic properties of sunscreen compounds such homosalate, red petrolatum, zinc oxide, N, N-dimethylamino benzoate, dioxybenzone, oxybenzone and dihydroxyacetone were examined[7]. The perceived stress scale (PSS) was used to gauge stress during the previous month. Using the Pittsburgh Sleep Quality Index (PSQI), the effectiveness of the sleep cycle was assessed. The patients' reports of an increase in the quantity, variety and severity of their acne lesions were used to identify an acne flare. Androgens, anticonvulsants (carbamazepine, phenytoin, gabapentin), antidepressants (lithium), antipsychotics, antitubercular drugs (isoniazid, pyrazinamide), antivirals (ganciclovir), over-the-counter medications like vitamin B12 and various vitamin supplements that are frequently linked to the onset or worsening of acne were also elicited.

On days 3-5 of the menstrual cycle, a number of hormones were measured using the random access fully automated immunoassay system (DXI-600, Beckman C), including total testosterone (TT), sex hormone binding globulin (SHBG), free androgen index (FAI), AMH, 17-hydroxyprogesterone (17-OHP), dehydroepiandrosterone sulfate (DHEAS) and follicle-stimulating hormone DHEAS and 17-OHP functioned as markers of the adrenal androgens while USG was used to evaluate PCOS. As a stand-in indicator of hyperandrogenemia, the free androgen index (FAI) was computed. Since it needs extremely sensitive equipment and is not standardized between laboratories or research, free testosterone was not evaluated.

Additionally, the transabdominal ultrasonography was performed on the same day as the blood sample using a curvilinear transabdominal probe (3 MHz, Medison-SonoAceX1). PCOS was diagnosed using the

Rotterdam criteria and biochemical hyperandrogenism was identified by serum TT levels more than or equal to 1.89 nmol L^{-1}.

Statistical methods: The data were entered into an MS EXCEL spreadsheet and analyzed using the Statistical Package for Social Sciences (SPSS) version 26.0.

While categorical data were supplied as number and percentage, continuous variables were presented as mean SD and median. The data were examined to see if they were normal using the Kolmogorov-Smirnov test. If normality was thought to be faulty, the nonparametric test was conducted.

The independent t-test/Mann-Whitney test was employed to evaluate quantitative variables between the two groups when the data sets were not regularly distributed. Qualitative variables were linked via Fisher's Exact and Chi-Square tests. The threshold for statistical significance was a p = 0.05.

RESULTS

In Table 1, the majority of acne patients (58.57%) were between the ages of 21 and 30, while just 4.28% were older than 40.

Table 2 shows that of the 70 adult female acne patients evaluated, 61.42% had late-onset acne and 38.57% had chronic acne.

In Table 3, Students, working women and housewives constituted 18.57, 37.14 and 44.28%, respectively in the study.

In Table 4, Papules were the most prevalent lesion at the time of presentation (61.42%), followed by mixed lesions, which included pustules and nodules.

Table 1: Frequency of age

Age (years)	No. women	Percentage
18-20	12	17.14
21-30	41	58.57
31-40	14	20.00
>41	3	4.28
Total	70	100.00

Table 2: Frequency of onset of acne

Acne	No. women	Percentage
Late onset acne	43	61.42
Persistent acne	27	38.57
Total	70	100.00

Table 3: Distribution of working women

Women	No. women	Percentage
Students	13	18.57
Working women	26	37.14
Housewives	31	44.28
Total	70	100.00

Table 4: Distribution of working women

Lesion	No. women	Percentage
Papule	43	61.42
Pustules	21	30.00
Nodules	6	8.57
Total	70	100.00

In Table 5, the patient acne severity was graded as mild (72.85%) to moderate (25.71%) and Severity (1.42%).

According to the subjective assessment, 21.3% of females showed a clear premenstrual flare (Table 6). The objective evaluation indicated that nutrition had a role in the condition of 23.33% of the patients, with "oily" and dairy-based diets and foods high in sugar and low in physical activity being prevalent. Fairness creams, foundations and facials were among the cosmetics that were at fault. While sunscreens had the highest maximum frequency per month, "fairness creams" were found to have the highest mean duration.

DISCUSSIONS

Although it has historically been thought of as a teenage illness, adult patients with acne are becoming more common. Similar to research by Layton *et al*.[1] and Khunger *et al*.[4] the majority of acne patients in our sample (58.57%) were between the ages of 21 and 30 whereas, just 4.28% were beyond 40[2]. In our analysis, the age range of 25-30 years included the majority of patients (71.7%). Of the 70 adult female acne patients we examined for our study, 61.42% had late-onset acne and 38.57% had chronic acne. In contrast, Dreno's findings show the opposite[3,4]. Where the majority began in adolescence. In line with earlier research, we discovered that persistent acne (53.3%) was more prevalent than late-onset acne (46.7%)[9]. Though Sardana. According to Mehta-Ambalal[5], late-onset acne is more prevalent than chronic acne (56.6%). In our study, 40% of patients had a history of acne in the family. From diverse research, this has been found in 10-56.8% of the cases[6] (Table 7).

In 45% of patients, there was seasonal exacerbation. Only two of them had winter aggravation, compared to 25 who did. A research from South India found that 44.5% of patients experienced seasonal exacerbation[7]. The development of comedogenic squalene peroxides and inflammation brought on by UV light may be the

Table 5: Distribution of Working women

Global acne grading system	No. women	Percentage
Mild	51	72.85
Moderate	18	25.71
Severity	1	1.42
Total	70	100.00

Table 6: Frequency table of subjective acne trigger factors

Aggravation factor	No. women	Percentage
Nil	45	64.3
Cosmetics	3	4.3
Drugs	2	2.9
Oily food	3	4.3
Premenstrual flare	15	21.3
Travel	2	2.9
Total	70	100.0

Table 7: Cosmetics usage in total acne population

Cosmetics usage	Mean±SD
Sunscreen use duration (month)	12.38±14.72
Sunscreen use frequency (days)	27.88±5.58
Fairness cream use duration (month)	31.90±36.63
Fairness cream use frequency (days)	26.99±9.72
Foundation use duration (month)	23.70±27.86
Foundation use frequency (days)	11.00±12.68
Facial duration (month)	9.61±7.41
Facial frequency (days)	2.29±0.51

Table 8: Hormonal analysis of total acne population

Hormones	Mean±SD
17OHP (ng mL^{-1})	2.60±0.73
DHEAS (µg mL^{-1})	2.99±0.94
TT (nmol L^{-1})	2.12±0.82
SHBG (nmol L^{-1})	55.65±36.44
FAI	3.99±5.36
AMH (ng mL^{-1})	6.19±5.29
LH (mIU mL^{-1})	7.78±5.49
FSH (mIU mL^{-1})	8.41±4.29
LH/FSH ratio	0.99±0.70
Prolactin (ng mL^{-1})	18.00±17.09
TSH (mIU mL^{-1})	4.90±2.9

TT: Total testosterone, 17OHP: 17-hydroxyprogesterone, DHEAS: Dehydroepiandrosterone sulfate, FAI: Free androgen index, AMH: Anti-Mullerian hormone, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone and TSH: Thyroid-stimulating hormone

cause of summer exacerbation. In our study, 50% of the patients complained of pain when exposed to sunshine[2,8]. Patients in 33.2 and 26.4% of cases, respectively, reported discomfort after exposure to the sun. Compared to our study, this was a little less.

Menstrual irregularity was reported in 25.8% of patients in an Indian research, which was greater than our study's rate[8]. In our study, 50% of the patients had premenstrual acne flare-ups. In 30-78% of instances, premenstrual flare has been seen. Our outcomes likewise fell inside this range. Between days 16 and 20 of the menstrual cycle, hydration-induced cyclical constriction of the pilosebaceous orifice may be the cause of premenstrual flare[9].

Additionally linked to the development of AFA is stress. varied studies may have varied amounts of pro-inflammatory cytokines and corticotrophin because to the different acne grading systems employed, as well as differences in the research population and geographic location. Due to end organ hypersensitivity, clinical hyperandrogenism symptoms such as hirsutism and rogenetic alopecia, irregular menstruation and hyperseborrhea may still occur. A substitute marker of peripheral androgen excess, cutaneous 5 reductase converts TT to DHT, which is then converted to 3 androstenediol glucuronide[10].

Our patients were all free of hirsutism. According to Seirafi *et al*.[2] and Tanghetti *et al*.[11], respectively, 5.7 and 2% of patients had hirsutism. In our analysis, there was just 1 patient with patterned alopecia. About 1.8% of individuals had androgenetic alopecia, according to Goulden *et al*.[10]. Acrochordons and acanthosis nigricans are thought to be indicators of insulin resistance[1]. In our study, 6.7% patients had acanthosis nigricans (AN) and 8.3% had acrochordons. There is just one research that looked at adult acne and discovered that AN was present in 5% of individuals[12].

We assessed 17-hydroxyprogesterone, Dehydroepiandrosterone Sulfate, Total Testosterone, Sex Hormone Binding Globulin, Free Androgen Index, Anti-Mullerian Hormone, Luteinizing Hormone, Follicle-Stimulating Hormone and Thyroid-Stimulating Hormone in terms of biochemical parameters. According to our study, 25% of the patients exhibited elevated LH. Balta conducted a case-control study. Between patients and controls, there was no statistically significant difference in mean FHS, according to Schmitt[13]. Sebum production, testosterone synthesis and bioavailability are all increased by insulin and IGF-1[14]. Raised insulin levels raise androgen levels, worsen acne and decrease sex hormone binding globulin (SHBG) concentration. Sterol response element binding protein 1 (SREBP1) is activated by IGF-1 to promote lipid production in sebaceous glands. The overactive SREBP1 promotes sebum production and raises the concentration of monounsaturated fatty acids in sebum, which promotes *Propionibacterium acnes* colonization and acne development[15]. In our study, 10% of the patients exhibited elevated serum insulin. Khunger. Compared to our study, Seirafi *et al*.[2] showed elevated LH in just 2 individuals. It might be attributed to dietary factors, hereditary factors, racial factors, smoking and socioeconomic status.

Since females are more likely to develop adult acne, underlying hormonal imbalances have been identified as a significant contributing factor. Dehydroepiandrosterone sulfate (DHEA-S), testosterone (TT) and DHT are androgens that control the genes that control sebaceous gland development and sebum production[16]. Sebaceous glands may be more susceptible to the effects of androgens or they may be directly affected by serum androgens. Different enzymes found in sebocytes and keratinocytes can locally produce TT and DHT. Pre-hormones (DHEA-S and rostenedione) are more readily converted peripherally into stronger androgenic hormones like TT and DHT[17].

In our study, 6.7% of patients had elevated serum TT. In other investigations, raised TT was discovered in 3.04-12.8% of patients[18]. In our study, participants with elevated serum FSH were 18.3%. Both Sardana and Bansal found that 1.6% of the individuals had

abnormal serum FSH. Raised LH levels were seen in just 3.3% of participants in our research. In a research from India, it was discovered that 4.1% of patients had elevated LH[19]. The LH/FSH ratio is around 1:1 during the follicular phase. One defining hallmark of PCOS is increased LH secretion. About 36.6% of the individuals in our study had an LH/FSH ratio greater than 1. 0.86-7.5% of patients had serum LH: FSH levels greater than 2[20]. In our study, a larger number of patients had elevated LH/FSH ratios. This could be because our study used a lower threshold for the LH/FSH ratio than did previous studies. About 15% of the individuals in our research had elevated serum TSH levels. This was comparable to a recent research from Nepal where 15.4% of individuals had elevated TSH[21]. Acne and hirsutism are examples of hyperandrogenic symptoms that women with hyperprolactinemia may exhibit. This might be because the adrenals are secreting more DHEA-S and less SHBG, which results in higher amounts of free TT[20].

CONCLUSION

Our study demonstrates that adult female acne may be brought on by nutrition, stress and cosmetics and that there is a specific hormonal environment responsible for hyperandrogenemia and elevated levels of adrenal androgen. We discovered that stress and sleep deprivation were both prevalent in a significant number of individuals with high levels of adrenal hormones, suggesting a shaky connection between stress and acne. We have also established that adult female acne patients had elevated AMH levels and more research on this hormone in adult acne patients is needed.

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