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TO EVALUATE THE TRIGGER FACTORS AND HORMONAL ABNORMALITIES IN ADULT FEMALE ACNE

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Abstract: ***Introduction:*** Acne is affecting an increasing number of adult females and so can no longer be considered as a disease of adolescence. Genetic and hormonal factors are thought to play key roles in the pathogenesis of adult female acne and the disease is characterized by a chronic evolution with frequent relapses requiring long-term maintenance therapy. ***Material and Methods:*** This is a prospective and observational study conducted over a period of 1 year. Patients over the age of 25 years presenting with acne in a tertiary care hospital were included in the study. A detailed history and examination was carried out, with a stress on aggravating factors. Hormonal imbalances were investigated in females with alopecia, obesity, hirsutism and menstrual irregularity. Severity of acne and complications like scarring and psychological stress were included. ***Results:*** Out of 90 patients included in the study 100% were women. The mean age of the patients was 31.2 years. Persistent acne was observed in 60%, while it was late onset in 40%. The most common lesion at presentation was papule (63.21%) followed by mixed lesions including pustules, nodules, and comedones. The patient acne severity was graded as mild (80%) to moderate (21%) with a mean GAGS of 13.45 ± 3.63. Facial involvement was seen in all, except two patients in whom only truncal involvement was present. On the face, cheek was the most common site involved (78.8%) followed by chin (58.8%), mandibular area (54.4%), forehead (41.5%) and nose (21.1%). ***Conclusion:*** Adult acne is predominant in women, and as compared to adolescent acne is more inflammatory, with involvement of the cheeks and lower half of the face, while comedones are rare.

Keywords: Acne, adult, inflammatory, women.

INTRODUCTION

Although acne is traditionally considered to be a disease which affects teenagers, recent research has shown that acne is affecting an increasing number of adults, particularly females (Chlebus, E., & Chlebus, M. 2017). This skin condition can have a substantial negative psychosocial and emotional impact on affected adults with older female patients reporting a greater impact of acne on their quality of life than younger patients (Uysal, G. *et al.,* 2017). Acne is characterized by the presence of inflammatory and non-inflammatory lesions and can lead to some degree of facial scarring in up to 20% of those affected with the likelihood of scarring increasing as the disease persists (Shrestha, S. 2018).

Acne is a common disease in adult females. The overall prevalence rates of adult female acne have been reported in different studies to range from 14% to 54% (Sardana, K. *et al.,* 2016). These variations in prevalence rates are likely to be due to differences in the design of the studies, with self-reported prevalence rates being higher than those from clinical studies.

There are two main subtypes of adult female acne. Persistent acne is acne which continues from adolescence into adulthood sometimes with periods of remission. This is the most common subtype of adult female acne being present in approximately 80% of cases (Kaminsky, A. *et al.,* 2019). Late-onset acne occurs in approximately 20% of women with adult female acne and this subtype has its first onset long after puberty, most often between the age of 21 and 25 years (Di Landro, A. *et al.,* 2016). Women with late-onset acne have significantly fewer comedones and a lower proportion of comedones than women with early-onset acne. Furthermore, adults with late onset acne often have larger pores than individuals of the same age without acne (George, R. M., & Sridharan, R. 2018).

The pathogenesis of adult female acne involves the interplay of excess sebum production, abnormal keratinization within the follicle and bacterial colonization of the pilosebaceous duct by Propionibacterium acnes (Romańska-Gocka, K. *et al.,* 2016). Hormonal

factors are also likely to play a role in the pathogenesis of adult female acne. Adult women with acne have worsening of their acne in the days before menstruation. The high frequency of seborrhoea in adult female acne also suggests that hormonal factors in association with genetic factors may be involved (Narang, I. *et al.,* 2019). However, studies of ovarian and adrenal androgenic hormone levels in the serum of adult females with acne have not shown any clear patterns of abnormalities (Bondade, S. *et al.,* 2019). Whilst several significant increases in androgen levels have been detected in women with adult-onset acne and hirsutism compared with healthy controls (e.g. luteinizing hormone, follicle-stimulating hormone, testosterone, dihydroepiandrosterone sulphate [DHEA-S]), only the level of DHEA-S was shown to be mildly to moderately elevated in women with adult-onset acne without hirsutism compared with controls (Dreno, B. *et al.,* 2011). The lack of androgen hormone abnormalities in adult female acne suggests that hormonal receptors expressed by both sebocytes and keratinocytes may be more sensitive to low levels of androgens in these patients and/ or there may be an increased local metabolism of androgens by enzymes (Chatzikonstantinou, F. *et al.,* 2019).

Materials And Methods

This is a prospective an observational study. The study was conducted over a period of 1 year. Patients over the age of 25 years presenting with acne vulgaris, attending outpatient department of dermatology in a tertiary care hospital were included in the study. Patients who were on hormonal therapy were excluded from study. Ethical clearance obtained from Intuitional Ethical committee. The patient reported trigger factors associated with acne flare were labelled as "subjective triggers" while objective evaluation of triggers was arrived by specific questions pertaining to diet, cosmetics, stress, and sleep pattern. A detailed history and examination was carried out for each patient, including a medical and family history. Information about the extent and site of involvement, aggravating factors including drug intake, sun exposure, and seasonal variation, application of cosmetics, stress, premenstrual flare and influence of pregnancy on acne was obtained.

Clinical assessment of each patient included type of acne lesions, distribution, severity and grading of acne. Associated findings such as obesity, hirsutism and alopecia indicating hormonal imbalance were also noted and investigations for polycystic ovarian disease and insulin resistance were done when indicated. Hormonal evaluation in terms of serum level of total testosterone, serum dehydroepiandrosterone (DHEAS), luteinising hormone (LH), follicular stimulating hormone (FSH) and prolactin (PRL) were done. Stress was evaluated through a questionnaire answered by the patient. A subjective assessment of its association with aggravation of the acne was made by the patient.

Statistical Analysis

Results were derived by simple statistical means of percentage and proportions.

Results

The study included 90 patients, 90 (100%) women. The most common lesion at presentation was papule (63.21%) followed by mixed lesions including pustules, nodules, and comedones. The patient acne severity was graded as mild (80%) to moderate (21%) with a mean GAGS of 13.45 ± 3.63.

The mean age of the patients was 31.2 years with a range of 26-50 years. The proportion of population of different age groups is detailed in Table 1. Most of the patients with acne (48.8%) were in the age range of 26–30 years while only 1.11% were aged between 46-50 years.

Table 1: Prevalence of adult acne according to age

Age group (years)	N=90(%)
26-30	44 (48.88)
31-35	31 (34.44)
36-40	12 (13.33)
41-45	3 (3.33)
46-50	1 (1.11)
>50	-

Table 2: Acne over face

Acne over face	N=90(%)
Cheek	71 (78.8)
Chin	53 (58.8)
Mandible	49 (54.4)
Forehead	41 (45.5)
Nose	19 (21.1)

In table 2, Facial involvement was seen in all, except two patients in whom only truncal involvement was present. On the face, cheek was the most common site involved (78.8%) followed by chin (58.8%), mandibular area (54.4%), forehead (41.5%) and nose (21.1%)

Table 3: Subtypes of female acne

Subtypes of female acne	N=90(%)
Persistent acne	54 (60)
Late-onset acne	36 (40)

In table 3, of the 90 adult female acne patients seen, 60% of females had Persistent acne and 40% presented as Late-onset acne.

Table 4: Frequency table of subjective acne trigger factors

Aggravation factor	Number of women	Percentage
Nil	60	66.67
Cosmetics	4	4.44
Drugs	6	6.67
Oily food	7	7.78
Premenstrual flare	12	13.33
Travel	1	1.11
Total	90	100

In table 4, Onset of acne due to drug use was found in only six cases (Two due to anti-tubercular therapy and one due to antipsychotic medications). Topical steroid use was found to be an important factor responsible for aggravation of acne in our study population. The objective assessment implicated the role of diet in 7.78% of patients with the common foods being "oily "and dairy products. The subjective evaluation revealed that 13.3% of females had a distinct premenstrual flare.

Table 5: Cosmetics usage in total acne population

Cosmetics usage	Sample size	Mean±SD
Sunscreen use duration (month)	4	11.62±3.35
Sunscreen use frequency (days)	4	23.83±3.62
Fairness cream use duration (month)	17	27.63±9.35
Fairness cream use frequency (days)	17	21.54±6.83
Foundation use duration (month)	13	19.5±3.52
Foundation use frequency (days)	13	8.54±3.73
Facial duration (month)	10	6.32±1.37
Facial frequency (days)	10	2.25±0.45

In table 5, among cosmetics; fairness creams, foundations, and facials were implicated. The mean duration was found to be the highest of "fairness creams" while the maximum frequency per month was highest for fairness creams. Females with persistent acne had a significantly higher frequency of foundation usage with a mean of 8.54 days per month.

Table 6: Hormonal analysis of total acne population

Hormones	Sample size	Mean±SD	Normal value
17OHP (ng/mL)	90	1.34±0.53	0.2-1.3
DHEAS (µg/mL)	90	1.64±0.34	0.48-2.75
TT (nmol/L)	90	1.01±0.69	<1.89
SHBG (nmol/L)	90	52.53±5.43	11.7-137.2
FAI	90	2.54±0.64	<5
AMH (ng/mL)	90	5.64±1.64	1.62-5.1
LH (mIU/mL)	90	5.54±1.54	0.8-15.5
FSH (mIU/mL)	90	6.64±1.34	1.3-23.4
LH/FSH ratio	90	0.86±0.09	<2
Prolactin (ng/mL)	90	17±5.54	3-18.6
TSH (mIU/mL)	90	3.1±1.7	0.5-5

Data were expressed as mean±standard deviation (SD). 17-OHP: 17-hydroxyprogesterone; DHEAS: Dehydroepiandrosterone sulfate; TT: total testosterone; SHBG: sex hormone-binding globulin; FAI: free androgen index; AMH: anti-Mullerian hormone; LH: luteinizing hormone; FSH: follicle-stimulating hormone; TSH: thyroid-stimulating hormone.

The hormonal analysis revealed that the mean values of all the hormones assessed in the study cohort were within the normal range as depicted in Table 6.

DISCUSSION

The mean age of adult females with acne in our study was 31.2 years which is akin to a previous study where the mean age of adult acne females was found to be 28.8 ± 3.64 years. (Berger, I. *et al.,* 2019) Most of our patients had mild to moderate acne which is consistent with previous studies (Saxena, U. *et al.,* 2018). Family history was noted in 10% of our study sample.

The premenstrual flare was the most common self-reported trigger factor (13.33%) which is less than the published literature wherein it ranges from 40% (Dreno, B. *et al.,* 2015) to 84.8% (Dréno, B. 2015). This factor is significant as it is the most convincing proof of elevated androgens and is a clinical manifestation of a relatively lower mid-cycle peak of estrogen in women with acne. We found that 7.78% of adult females had a history of regular intake of oily foods. Landro *et al.,* reported that 50% of adult acne patients consumed milk and dairy products regularly and further highlighted that the rate of affected women consuming vegetables, fruits, and fish was significantly less than the normal population (Zeichner, J. A. *et al.,* 2017). Chatzikonstantinou F and Cinar N Cetinozman F also observed that oily foods and dairy products precipitated acne in 37.3% and 1.8% adult acne patients, respectively (Silpa-Archa, N. *et al.,* 2017). Diet has been propounded to cause acne via deranged nutrient signalling-induced hyperkeratosis and hyperseborrhea (Auffret, N. *et al.,* 2016). This with over-activation of mTORC1 by a high glycaemic diet can cause acne in conjunction with increased levels of androgens (Bhat, Y.J. *et al.,* 2017).

Various cosmetics implicated in acne included sunscreens, fairness cream, foundation, and facials. It has been historically believed that low-grade persistent acne in females could occur majorly due to cosmetics use which leads to the use of the term "acne cosmetica". A hospital-based study noted that 40% of adult acne patients experienced an aggravation of lesions after cosmetic use which was supported by another study, which also concurred that a statistically significant difference in acne severity between "make-up" users and nonusers was seen (Antiga, E. *et al.,* 2015). Significantly, females with persistent acne were found to have a higher use of foundation. This is an important and overlooked cause and may play a role in persistent acne. This is in consonance with the Chlebus study where a significant correlation was seen between acne and the use of "full cover foundation (Del Rosso, J. Q. *et al.,* 2015)." While a variety of cosmetic ingredients are known to be comedogenic and it is believed that many cosmetic companies now replace these ingredients with non-comedogenic alternatives (Rocha, M. A., & Bagatin, E. 2018). Though sunscreens were a minor cause, they have been well-established as a cause of "acne cosmetica"and should be considered in our population. Here it must be noted that it is the vehicle that is the culprit and this is compounded by the enhanced comedogenicity with concomitant UV radiation which is one of the possible causes of the reported summer flare in acne (Goulden, V. *et al.,* 1999).

Biochemical hyperandrogenemia can be studied by analysing the deranged values of TT, FAI, 17-OHP, and DHEAS as these can assess both the ovarian and adrenal sources of androgens. The elevated values of DHEAS (17.5%) and FAI (15.83%) are consistent with a previous study by (Zouboulis, C. C. *et al.,* 2016) who observed that DHEAS was raised in 18.5% acne patients and SHBG was low in 33.8% in acne females, the latter accounting for the increased FAI. Zouboulis CC, also noted a higher prevalence of raised testosterone and low SHBG in 46% of adult females with persistent or late-onset acne (de Medeiros Ribeiro, B. *et al.,* 2015). Also found that testosterone and DHEAS were raised in 24% and 30% patients, respectively (Dreno, B. *et al.,* 2015).

The high level of 17-OHP in our work was above the reference range in 66.67% adult females though none of them had a value higher than 8 ng/mL which is considered diagnostic of non-classic congenital adrenal hyperplasia (NCCAH). A study by George *et al.,* concurred that a value of more than 4 ng/mL has a sensitivity of 90% in diagnosing NCCAH (Kang, D. *et al.,* 2015). In our work, only 10% and 1.66% patients had a value >2 ng/mL and >4 ng/mL, respectively. The high value of 17-OHP in our work is comparable to other studies that have analysed this hormone in acne which concurred that 17 OHP can be elevated in 31% patients of acne alone and in 40% patients of acne with (Gold, L. S. *et al.,* 2016)

Our hormonal milieu is significant for two reasons. Apart from the accepted role of androgens in stimulating the sebaceous gland, our work supports the porosities that chronic stress leads to enhanced secretion of adrenal androgens, resulting in sebaceous hyperplasia and the subsequent induction of acne (Thielitz, A. *et al.,* 2015). This is more so as the adrenal gland is intricately linked to stress, which has been, in turn, found to be a trigger for acne and this possibly accounts for the raised adrenal hormones (Kainz, J. T. *et al.,* 2016). Significantly, 42.8% of patients with elevated DHEAS and 58.75% with raised 17-OHP had a documented history of moderate to severe stress.

CONCLUSION

Thus, our work shows that adult female acne may be triggered by diet, stress, and cosmetics, and there is a distinct hormonal milieu that accounts for hyperandrogenemia and the increased adrenal androgen levels. We have also reconfirmed the raised levels of AMH in adult female acne and this hormone should be studied further in adult acne females.

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