

Correlation of Hormonal Profile and Lipid Levels with Female Adult Acne in a Tertiary Care Center of Nepal

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ABSTRACT

Background: Acne beyond 25 years of age is frequently associated with hormonal derangement in women. Hormonal association provides the impetus for hormonal therapy as well as underpins the need for blood investigations in this population. Hence, we aim to estimate the presence of hormonal derangement and lipid alteration in female adult acne.

Methods: A prospective, observational study was conducted in Dhulikhel Hospital from July 2015 to February 2016. Females older than 25 years with acne were taken in the study after informed consent. Total 100 patients were enrolled after sample size estimation. Hormonal panel and lipid profile were measured. Hormones tested were androgens, C-peptide and thyroid stimulating hormone. Data analysis was done with SPSS-23. Bivariate analysis was done by chi-square test for categorical data.

Results: In this study, majority of patients were younger than 30 years (70.5%) and perioral area most commonly involved. Hormonal alteration was seen in 37.2% patients, among which 17.9% had hyperandrogenism, 15.4% had abnormal thyroid level and 10.3% had high C-peptides respectively. Lipid profile was altered in 15.4% patients. Hormonal alteration had significant association with irregular menstruation ($P < 0.05$) but not acne severity.

Conclusions: We observed hormonal alteration frequently in females with adult acne, which comprised of various hormonal parameters including hyperandrogenism. Hormonal alteration reflects deranged metabolic milieu and we suggest that wide hormonal panel should be done in female adult acne. Relationship of hormones with menstrual irregularity but not with acne severity, suggest that clinical symptoms should lead hormonal investigations in all grades of acne.

Keywords: Acne; adult; hormones; lipid; thyroid.

INTRODUCTION

Acne persisting or occurring after 25 years of age is adult acne or post-adolescent acne.¹ With female predominance, it affects 12-22% women between 25 to 50 years age.^{2,3}

Etiopathogenesis is multifactorial. Hormones implicated are androgens, estrogen, insulin, glucocorticoids, prolactin, etc. Hyperandrogenism (HA) can be ovarian or adrenal in women and Polycystic ovarian syndrome (PCOS) contributes to >90% of such cases.⁴ Adult acne is frequently linked with hormonal alterations.⁴⁻⁷ Adult acne without hormonal imbalance, suggests end organ hypersensitivity to normal androgen levels.^{3,4}

Since androgens are derived from plasma cholesterol, lipid alteration might cause acne.⁸ In adult acne,

evidence for both deranged and normal lipid profile exists.⁹⁻¹¹ Similarly, thyroid disorder may be related to acne. Acne comprises of 5% of skin changes in patients with thyroid disorder.¹² However, thyroid changes in post-adolescent acne is controversial.^{13,14} Hence, this study was conducted to look for alteration in various hormonal parameters in female adult acne.

METHODS

A prospective, observational study was conducted in Department of Dermatology, Dhulikhel Hospital-Kathmandu University from July 2015 to February 2016.

Female patients older than 25 years, presenting with acne were included. Total of 100 patients were enrolled in the study. Sample size was calculated based on reported prevalence of approximately 50% of cases with

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associated hormonal derangement in adult acne.^{5,6}

$p=0.5$ (probability), $q=0.5$ (1-p), Allowable error(d) = 20% of $p=0.1$, Sample size = $4pq/d^2=100$

Clinico-epidemiological data was noted. Assessment of acne severity was based on grading the clinical morphology of lesions.¹⁵ All patients underwent investigations for androgens, insulin, thyroid and lipid levels. Blood was tested on the next day, early morning, on empty stomach and reports were collected same day.

Inclusion Criteria: Female patients 25 years of age or older, presenting with acne. Exclusion Criteria: Patients under treatment for acne, those with history of topical creams or cosmetics, contraceptives device usage, taking lipid lowering drugs, pregnancy, lactation, history of cardiovascular disease and history of smoking.

Parameters included were total testosterone(TT), sex hormone binding globulin(SHBG), Dihydroepiandrosterone sulfate(DHEAS), ratio of Leutinizing hormone(LH) to Follicle stimulating hormone(FSH), thyroid stimulating hormone(TSH), C-peptide and fasting lipid profile. LH:FSH ratio of $>2:1$ was considered abnormal.¹⁶ CLIA(chemiluminescent immunoassay) technique was used for hormonal measurement. CLIA is sensitive, automatable, fast and cheap. LIAISON[®] machine from DiaSorin brand was used. Standard laboratory values in Dhulikhel Hospital laboratory were taken as reference range. Lipid profile was estimated with dry chemistry analyzer. Cut off values for Dyslipidemia was taken according to National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) criteria.¹⁷

Approval from the Institutional Review Board was taken prior to the study. Informed consent was obtained from all patients. Data analysis was done with SPSS version 23. Bivariate analysis was done by chi-square for categorical data.

RESULTS

Among 100 patients enrolled, 78 patients (response rate 78%) reported to us with results of blood investigations. The mean age of our patients was 28.8 ± 3.64 years, with the age range of 25-40 years. Majority of the patients (70.5%) were between 25-29 years of age, and only 10.3% were older than 35 years. Duration of lesions varied from 3 weeks to 10 years. Persistent acne was seen in 55(70.5%) patients and late onset in 26(33.3%) patients. Table 1 given below shows descriptive analysis.

Among all, 64.1% patients had acne grade II, followed by grade III (21.8%), grade I(10.2%) and grade IV(3.8%) acne.

Perioral area and chin was most commonly involved (41%). Other areas affected were cheeks, forehead, neck and trunk. Irregular menstrual cycle was seen in 24(30.8%) patients.

Table 1. Showing descriptive variables (n=78).

Age		
25-29 years	55 (70.5%)	Mean=28.28 years
30-34 years	15 (19.2%)	
35-39 years	7(9.0%)	S.D = 3.64
40-45 years	1(1.3%)	
Site		
Perioral	32(41%)	
Upper face (cheeks and forehead)	31 (39.7%)	
Neck and trunk	15 (19.2%)	
Severity of acne		
Grade I	8 (10.3%)	
Grade II	50 (64.1%)	
Grade III	17 (21.8%)	
Grade IV	3 (3.8%)	

Table 2. Hormonal panel and lipid profile.

Parameter (n=78)	No of patients (%) with derangement	Hyperandrogenism	Hormonal alteration
TT	10 (12.8%)	14(17.9%)	29 (37.2%)
SHBG	4 (5.1%)		
DHEAS	1 (1.3%)		
LH:FSH ratio (>2:1)	8 (10.2%)		
C-peptide	8(10.3%)		
TSH	12(15.4%)		
Lipid profile	12 (15.4%)		

Hormonal alterations were noted in 29(37.2%) patients(Table 2). Among them, hyperandrogenism was found in 14(17.9%) patients. Lipid alteration(15.4%) comprised of increase in total cholesterol(TC=7.6%), Low density lipoproteins (LDL=3.8%), triglycerides (TG=5.1%) and decrease in high density lipoproteins (HDL=10.2%). Some patients had abnormal levels of more than one biochemical parameter. Table 2 shows frequency of patients with abnormal blood parameters. Menstrual irregularity had statistically significant association with hormonal alteration ($P=0.038$) (Table 3), but not with hyperandrogenism (Table 4). Hormonal derangement or hyperandrogenism was not associated with severe acne (Table 5, Table 6).

Table 3. Hormonal alteration and menstrual cycle.

Hormones (n=78)	Menses		Total	P value
	Regular	Irregular		
Normal	38	11	49	0.038
Altered	16	13	29	
Total	54	24	78	

Table 4. Hyperandrogenism and menstrual cycle.

Hyperandrogen- ism (n=78)	Menses		Total	P value
	Regular	Irregular		
Absent	46	18	64	0.28
Present	8	6	14	
Total	54	24	78	

Table 5. Hormones and acne severity

Hormone (n=78)	Acne Severity (Grade)				Total	P value
	I	II	III	IV		
Normal	7	34	7	1	64	0.066
Altered	1 (12.5%)	16 (32%)	10 (58.8%)	2 (66.7%)	14	
Total	8	50	17	3	78	

Table 6. Hyperandrogenism and acne severity.

Hyperandrogenism (n=78)	Acne Severity (Grade)				Total	P value
	I	II	III	IV		
Absent	7	44	11	2	64	0.15
Present	1 (12.5%)	6 (12%)	6 (35.3%)	1 (33.3%)	14	
Total	8	50	17	3	78	

DISCUSSION

Acne is a disorder of adolescents. However, its prevalence among post-adolescent population is rising. Studies report adult acne in up to 60% of patients, with 10% patients between 35 to 44 years of age.^{1,3}

The mean age of the patients in our study was 28.8±3.64 years, slightly younger than previous reports with mean of 30-35.5 years.^{1,6-18} Adult acne is persistent or late onset. Persistent acne is continuation of adolescent acne beyond 25 years of age, while late onset acne begins after 25 years.¹⁸ In our study, persistent acne occurred in 70.5% cases and late onset in 33.3% patients, consistent with previous findings.^{7,18} Goulden et al. suggested that true late onset acne may represent abnormal androgen metabolism.¹ Sporadic acne and recurrent acne have also been described but their association with hormones is ill-defined.⁷ Premenstrual flare is common in adult acne, seen in 44-78% cases.^{19,20} Older women (>33 years) report premenstrual flare more than 22-33 years old.²⁰ We haven't noted entities like premenstrual flare or recurrent acne.

Skin lesions in adult acne commonly occur in perioral and lower face distribution.^{1,18-21} In our study, commonest site was lower face (41%) while Khunger et al. found commonest involvement of cheeks(81%) followed by lower face.¹⁸ Morphology of adult acne is inflammatory and low grade, while adolescent acne is comedonal.

In accordance, our study had grade II acne(64.1%) in majority of the patients.^{1,8,18} Capitano et al. reported predominantly comedonal morphology in adult acne with strong correlation with smoking.²¹

Factors affecting female adult acne are family history, smoking, cosmetics, obesity, hormones, stress, diet, etc.^{1,21,22} Androgens are key hormones regulating sebum production and follicular hyperkeratosis. Androgen-insensitive individuals do not produce sebum and do not develop acne. LH regulates androgen secretion by ovaries. Estrogen decreases sebaceous gland size and sebum production.^{3,4} While androgens have clear roles in acne pathogenesis, research continues on the role of estrogen.

Insulin directly stimulate sebocyte proliferation, increase androgens, inhibit SHBG, stimulate 5 α reductase enzyme and enhance lipogenesis. It increases insulin like growth factors(IGF-1), which alter androgens as well as keratinocyte proliferation. Hence both insulin and IGF-1 have comedogenic effect.^{4,23} Likewise, cholesterol is a precursor of androgens, rise in total cholesterol is linked with acne. Androgens in turn, increase hepatic lipase activity, thus increasing HDL catabolism.¹⁰ Furthermore, insulinotropic palaeolithic diets are extrinsic factors for insulin resistance leading to acne.^{22,23}

Hyperandrogenism, insulin resistance and thyroid disorders positively correlate with adult acne, and also

independently with each other. Dyslipidemia is closely linked insulin resistance and hypothyroidism.^{3,4,23} PCOS is commonest endocrine disorder in women, with mild elevation of testosterone, hyperinsulinemia, dyslipidemia and elevated LH:FSH ratio.²⁴ There is low grade chronic inflammation, propagating a vicious cycle of hormonal imbalance and acne in these patients.⁸

In view of role of hormones, review articles suggest a wide hormonal panel tests in female adult acne, but most studies are based on androgen profile.^{3,4,7} Others have included endocrine parameters such as prolactin, estradiol, progesterone, serum cortisol, insulin and thyroid antibodies.^{9,10} There is no standard protocol for hormonal profile yet. Hormonal evaluation is indicated in those with late onset or persistent acne, menstrual irregularity, clinical signs of androgen excess or resistant to therapy.^{4,7}

In our study, hormonal alteration occurred in 37.2% patients and hyperandrogenism in 17.9% patients. Addor et al had hormonal alteration in 49.7% of their patients.⁶ HA was seen in 28.6%-70% patients with acne.^{5,10} Khunger et al. from India had hyperandrogenism in only 3.04% of their patients. They found altered TT, LH:FSH ratio, increased insulin but no change in DHEAS or SHBG similar to our study.¹⁸ Others show elevated TT and DHEAS in adult acne. There are reports with normal or "high-normal" levels of TT and DHEAS as well. Levels of SHBG are inconsistent, with raised, normal or decreased levels in different studies.^{10,25} This lack of consistency in prevalence and pattern of hyperandrogenism in adult acne is probably because of external triggers described earlier and different clinical profile of patients in these studies. Acne in patients with hirsutism, obesity and irregular menstrual cycle had more evidence of hyperandrogenism.^{5,9,26} In our study, there was significant association of menstrual irregularity with altered hormonal profile ($P < 0.05$), while its association with hyperandrogenism was not significant. Severity of acne was not associated with hyperandrogenism or total hormonal profile as reported by Cibula et al.²⁷

Lipid profile was altered in 15.4% of our patients, with low HDL (10.2%) as the commonest derangement. Studies show alteration of lipid profile in acne similar to PCOS, with rise in TC and LDL and decrease in HDL.^{8,9} Lipid alteration has also been noted in non-obese, non-hirsute acne patients, but there are reports with normal lipid profile in acne.^{10,11} It is important to look for other risk factors such as diet, obesity or coexisting illness before determining casual association of lipid profile with adult acne.

In our study, C-peptide was altered in 10.3% patients. C-peptide is a measure of endogenous insulin secretion and is more stable than insulin.²⁸ Although insulin is indirectly associated with acne as described earlier, Balta et. al did not find its major role in the pathogenesis of adult acne.²⁹ Another study showed insulin resistance common in male postadolescent acne.³⁰ Hence, data is not conclusive so far, but our study provides an impetus for future research.

TSH was altered in 15.4% of our patients. While Vergou et al. found significant correlation of thyroid antibodies with adult acne, Ekiz et al. reported no association with thyroid profile.^{13,14} Since percentage alteration in TSH is comparable with HA and lipid levels in our study, we suggest TSH be included among screening tests.

It is noteworthy that screening for thyroid and insulin resistance besides androgens, doubled the frequency of hormonal alteration in our study. Moreover, wider hormonal panel advised in literature is not included in our study, which would perhaps detect wider endocrine abnormalities. Moreover, we had not enrolled healthy age matched controls to compare their hormonal profile with, which is a limitation of this study.

CONCLUSIONS

Role of hormones in adult acne has been reiterated in time. However, there is no strict consensus or guidelines yet. Although recent reviews on adult acne doesn't strictly require hormonal alteration in order to start hormonal therapy, biochemical evidence of hormonal derangement can guide the line of treatment. We observed hormonal alteration frequently in females with adult acne, which comprised of various hormonal changes besides hyperandrogenism. Hence we suggest that a wide array of hormonal alteration might lead to adult acne. Moreover, relationship of hormones with menstrual irregularity but not with acne severity, suggest that clinical symptoms should lead hormonal investigations in all grades of acne. We suggest that dermatologists should consider hormonal alterations in patients with acne persisting after 25 years of age, especially in women.

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