A prospective study of correlation between hormonal profile and acne vulgaris in adult patients

MSN Murthy¹, Kadi Ramesh^{2,*}

¹Associate Professor, ²Assistant Professor, Dept. of Dermatology Venereology and Leprology, Konaseema Institute of Medical Science Amalapuram Andhra Pradesh, India

*Corresponding Author:

Email: drrameshderma@gmail.com

Abstract

Introduction: Although various studies has been conducted regarding pathogenesis of acne vulgaris and proved it to be multi factorial, but there is strong association between acne vulgaris and hormone profile of patients. Present study has been designed to document and access the correlation between hormone profile and acne vulgeris, with a primary aim to know the hormonal profile of acne vulgaris patient and correlate the hormone level with acne vulgaris patients.

Materials and Methods: This study is prospective randomized case control study conducted in the dept. of dermatology venereology and leprology Konaseema institute of medical science Amalapuram Andhra Pradesh from August 2015 to April 2018. In present study 80 clinically diagnosed, acne vulgeris patients were randomly selected for this study based on inclusion and exclusion criteria. Another 80 age and sex matched healthy volunteers were taken as control group who are free from acne.

Result: Mean serum concentration of testosterone was 83.54 ± 28.31 ng/dl in cases, but in control group mean serum concentration was 48.89 ± 38.79 ng/dl, with P value 0.00001. Mean of serum DHEAS concentration was 265.79 ± 53.48 , mcg/dl in patients but in healthy volunteers it was 211.48 ± 36.11 mcg/dl, with P value 0.00012.

Serum insulin level in acne patients were (mean \pm SD) 7.163 \pm 1.843, mIU/L but in control group it was 5.48 \pm 1.24 mIU/L with P value 0.0019. Mean concentration of serum glucocorticoid was 14.63 \pm 3.24mcg/dl in cases but in control it was 13.42 \pm 4.94 mcg/dl having P value 0.89. Serum IGF-1 mean value was 272.62 \pm 62.32 ng/ml in cases, and 246.76 \pm 70.32ng/ml in control with P value 0.074. Serum ACTH concentration was 39.66 \pm 4.24pg/ml in cases (mean +SD) but in control 33.60 \pm 9.92pg/ml with P value 0.0035.

Discussion and Conclusion: Serum concentration of testosterone, DHEAS, ACTH and IGF-1 level was higher in acne vulgeris cases then control which indicate a correlation between these hormone and acne vulgeris. Increase in serum level of insulin and HOMA-IR value suggests an insulin resistance state in acne vulgeris. We have also found a correlation between PCOS and acne vulgeris.

Keywords: Hormonal profile, Acne vulgaris, Adult patients.

Introduction

The sebaceous gland is a holocrine secreting tissue present in skin. Main function of this gland is to excrete sebum, which coat the skin as a hydrophobic protection and heat insulation.¹ Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit. It is a common disease of skin affecting more than 80% of female predominance.² adolescent with Pathophysiology of acne vagaries is characterised by, over production of sebum, formation of comedones, erythematous papules, pustules, and some cases accompanied by scarring. The pathogenesis of acne vulgaris is multifactorial, which include release of inflammatory mediators in the skin, proprionibacterium acnes follicular colonisation, Toll like receptors, hyper keratinisation, increase follicular sebum excretion, alteration in composition of lipid, change in oxidant/anti-oxidant ratio characteristic of lipid in skin, diet, and hormones.^{3, 4} It has been found recently that matrix metalloproteinase and relative nuclear deficiency of the nuclear transcription factor foxol appear to play role in pathogeneses also.^{5, 6}

But in addition to all these finding there is a strong association between the hormone and acne vulgaris, As per the article published in dermato endocrinology by wen- chieh chen the skin is considered as an endocrine organ and pilosebaceous gland is the main factory of hormone production.^{7,8} Several hormones are responsible for the regulation of the activity of sebaceous gland like, androgen, estrogen, progesterone, Insulin/ insulin like growth factors, adreno lontico trophic hormone, glucocorticoids, FSH and LH. These hormones directly or indirectly contributes in the pathogenesis of Acne vulgarise.

Androgen: Studies have proved the statistically significant increase in circulating androgen level in women with acne, and its aggravation during menstruation and hyper androgenic state. It has also been hypothesized that patient with acne have more active 5α – reductase type-1 and have greater activity of 17ß hydroxysteroid dehydrogenase activity which is associated with abnormal hyper proliferation of keratinocytes.⁹

Estrogen: A low serum level of estrogen is associated with acne vulgaris, 17 β - estradiol plays in important role by inhibiting chemokine RANTES and interferon y induced 10kDa protein, by which it play anti-inflammatory role.¹⁰

Glucocorticoids and ACTH: It has also been proved that steroid induced Toll-like receptor-2 along with

P.acne plays impotent role in exacerbation acne vulgaris.

Insulin/ insulin like growth factor: The decrease in insulin sensitivity increases the free androgen index. Studies has proved that increased insulin and increased IGF-1 has been found in women and men with acne, which associates the possibility of role of GH, Insulin and IGF-I in acne.¹¹

Polycystic ovaries are most common endocrinological disorder which is associated with acne vulgaris. PPARs regulate the energy homeostatic by modulating glucose and lipid metabolism also found to regulate cellular function in skin. Decreased PPAR_Y level and signalling is found in patients with acne vulgaris.¹²⁻¹⁴

Although various studies has been conducted regarding pathogenesis of acne vulgaris and proved it to be multi factorial, but there is strong association between acne vulgaris and hormone profile of patients. Present study has been designed to document and access the correlation between hormone profile and acne vulgeris, with a primary aim to know the hormonal profile of acne vulgaris patient and correlate the hormone level with acne vulgaris patients.

Materials and Methods

This study is prospective randomized case control study conducted in the dept. of dermatology venereology and leprology Konaseema institute of medical science Amalapuram Andhra Pradesh from August 2015 to April 2018.

Studied Population: In present study 80 clinically diagnosed, acne vulgeris patients were randomly selected for this study based on inclusion and exclusion criteria. Another 80 age and sex matched healthy volunteers were taken as control group who are free from acne. Divided in two groups Group A consist of 80 clinically diagnosed cases of acne vulgeris and group B consist of 80 healthy volunteer.

2. Both sex

Exclusion Criteria

- 1. Pregnancy and lectors
- 2. Oc pills
- 3. Smoking and alcohol
- 4. Malignancy
- 5. Diabetic and lipid animalises

Laboratory Investigations: A part from normal routine investigation hormonal profile was done for both patients and control. Venous blood samples were collected for assay in early morning from all the study population. From women blood sample were collected during the follicular phase between the second and the fourth day of menstrual cycle. Venous blood once aspirated was kept in plain test tube, allowed to clot for 20 to 30mins, then centrifugation at 2500rpm for 10min and stored at -20°c.

Parameters investigated include, testosterone, (ng/dl), Dehydroepiandrosterne sulphate, (mg/dl), glucocorticoid (mg/dl), ACTH (pg/ml), insulin like growth factor (ng/ml), serum insulin (mlU/L), estradiol (pg/ml). For estimation of these parameters COBAS e 411 immunochemistry analyser was used. HOMA-IR was calculated by using formula FPI X FPG/22.5.¹⁵ Hexokinase method was used for estimation of fasting plasma glucose.

Ethics: Before start of this study approval was obtained from institutional ethics committee and a written informed consent was obtained from each patient before enrolment of them for study. All the participants were properly explained the study requirements.

Statistical Analysis: The data was analysed by using SPSS 16.0 software. The parametric data was analysed by unpaired T-test and non-parametric data was analysed by chi-square test. P value <0.05 was considered statically significant.

Result

Inclusion Criteria:

1. Age- 14 to 40yrs

· Demographic variables					
	variables		Group A (n=80)	Group B (n=80)	P value
	Age mean		23.046 <u>+</u> 7.368	24.12 <u>+</u> 8.81	0.269754
	sex	Μ	42	51	Chi square statistic
		F	38	29	2.0799 0.14928
	$BMI(kg/m^2)$		25.21 <u>+</u> 2.19	23.12 <u>+</u> 3.789	0.00001

 Table 1: Demographic variables

As per table -1 mean age of the patients was, 23.048 ± 7.368 yrs and in control group it was 24.1219 ± 8.81 yrs having P value 0.269754. Sex distribution of the patient was also comparable to each other statistically in both groups with P value 0.14928. Body mass index of the patient was 25.21 ± 2.19 kg/m² and in control 23.12 ± 3.789 kg/m² this is significantly higher than control with P value 0.00001.

IP Indian Journal of Clinical and Experimental Dermatology, April-June, 2018;4(2):151-155

Table 2. Chinear characteristic of cases	Table 2:	Clinical	characteristic	of cases	
--	----------	----------	----------------	----------	--

	variables	Finding(number and mean)	
Disease duration (in years)		0.876 <u>+</u> 0.4839	
	Mid face	18	
site	cheeks	20	
site	Mid face and cheeks	32	
	back	10	
	comedones	10	
Type of	Papules and pustules	48	
	nodules	22	

As per table 2, mean duration of disease was 0.876 ± 0.48 39 yrs. Eighteen patients have lesion on the mid face, in 20 patients it was on cheeks, thirty two patient has lesion on mid face and cheek both, only 10

patients have lesion on back. In 10 patients comedones were type of lesion, papules and pustules are present in 48 patients, but 22 patients were presented with nodules.

 Table 3: Comparison of hormone concentration between case and control

Parameters	Group A (mean+ SD)	Group A (mean+ SD)	P value
Testosterone(ng/dl)	83.54 <u>+</u> 28.31	48.89 <u>+</u> 38.79	0.00001
DHEAS(mcg/dl)	265.79 <u>+</u> 53.48	211.48 <u>+</u> 36.11	0.00012
Insulin(mIU/dl)	7.163 <u>+</u> 1.842	5.48 <u>+</u> 1.24	0.0019
Glucocordicads(ug/dl)	14.63 <u>+</u> 3.24	13.42 <u>+</u> 4.94	0.89
IGF(ng/ml)	272.62 <u>+</u> 62.32	246.76 <u>+</u> 70.32	0.074
ACTH	39.66 <u>+</u> 4.24	33.60 <u>+</u> 9.92	0.0035
HOMA-IR	2.82 <u>+</u> 0.46	1.98 <u>+</u> 0.63	0.0014
Estradiol(pg/ml)	49.05 <u>+</u> 14.09	64.42 <u>+</u> 16.79	0.0059

Regarding comparison of hormone concentration between case and control, mean serum concentration of testosterone was 83.54 ± 28.31 mg/dl in cases, but in control group mean serum concentration was 48.89 ± 38.79 mg/dl, with P value 0.00001. Mean of serum DHEAS concentration was 265.79 ± 53.48 , mcg/dl in patients but in healthy volunteers it was 211.48 ± 36.11 mcg/dl, with P value 0.00012.

Serum insulin level in acne patients were (mean \pm SD) 7.163 \pm 1.843, mIU/L but in control group it was 5.48 \pm 1.24 mIU/L with P value 0.0019. Mean

concentration of serum glucocorticoid was 14.63 ± 3.24 mcg/dl in cases but in control it was 13.42 ± 4.94 mcg/dl having P value 0.89. Serum IGF-1 mean value was 272.62 ± 62.32 ng/ml in cases, and 246.76 ± 70.32 ng/ml in control with P value 0.074. Serum ACTH concentration was 39.66 ± 4.24 pg/ml in cases (mean +SD) but in control 33.60 ± 9.92 pg/ml with P value 0.0035.

Mean serum estradiol concentration in acne patients were 49.05 ± 14.29 Pg/ml but in control group it was 64.42 ± 16.79 pg/ml. With P value 0.00059.

Table 4: Correlation of PCOS in cases and healthy control

	Cases n=80)	Control (n=80)	P value
pcos	8	1	Chi square statistic =5.7689 P value = 0.01632

8 patients in acne vulgaris group were diagnosed to be PCOS but only one patient in control having PCOS and this finding was statistically significant with P value 0.01632.

Discussion

The acne vulgaris is a chronic inflammatory disease of pilosebaceous unit, having multi factorial pathogenesis. Studies have proved that in the skin pilosebaceous unit is the site of production of hormone. Various enzymes required for synthesis of hormone and receptors of various hormones are present in these pilosebaceous unit. An imbalance in the homeostasis of this dermato-endocrinological milieu is considered as etiological factor for acne vulgaris and proper understanding of this is essential for selection of therapeutic options, Chen WC et al.⁷

In current study age and sex matched (P=0.2 69754, P= 0.14928) patient were enrolled, out of that 80 were cases and 80 were control that is healthy persons without acne. We have found that BMI (kg/m2) was significantly higher in acne group then control with P value 0.00001.which is corroborated with the finding of Tsai me et al, population based study of Halvorsen et al has also supported our study, but the study of P.H.Lu. et al of Taiwan has found negative association between acne and BMI.¹⁶⁻¹⁸

Regarding hormonal profile and its correlation with acne vulgaris, we have found that the serum concentration of testosterone was significantly higher in acne vulgaris group then control having P value 0.00001. Similarly the concentration of DHEAS was also significantly higher in cases than control. A Hatwal et al have found that in acne vulgaris group serum testosterone was partially increased but DHEAS level was significantly increased, this study partially support our study, But our study corroborates with the study of Yang XQ et al.^{19,20}

Serum fasting plasma insulin concentration was significantly higher in acne vulgaris patient in comparison to control. HOMA-IR value was also significantly higher in acne vulgaris group. This finding suggest that there exist insulin resistance along with acne vulgaris this finding totally corroborates with the study of Nazam Emiroglu et al.²¹

Michela Del Prete et al concluded in has study that there is metabolic imbalance in patient with acne, and insulin resistance seems to play the main role for development of acne.²² But the study of Prathima et al found very weak association between insulin resistance and acre vulgaris.²³

In current study serum glucocorticoids level was statistically comparable in both group. But serum ACTH level was significantly higher in case then control, this is supported by the work of Shibata et al and Scholzen et al.^{24,25}

In present study we have also found that serum Estradiol. Concentration was significantly low in case then control. Which corroborates with the finding of ola Ahmed Bakry et al^{26}

We have found a statistically significant association between PCOS and acne vulgeris. A study of 60 cases by Iurassich S et al supports our finding. Our study is also corroborates with the work with Sayera Begam et al, she has concluded that all women with acne should be considered for underlying PCOS and asked about their menstrual patterns and examined for other sign of hyperandrogenism.^{27,28}

Conclusion

We would like to conclude that serum concentration of testosterone, DHEAS, ACTH and IGF-1 level was higher in acne vulgeris cases then control which indicate a correlation between these hormone and acne vulgeris. Increase in serum level of insulin and HOMA-IR value suggests an insulin resistance state in acne vulgeris. We have also found a correlation between PCOS and acne vulgeris.

References

 Simpson NB, Cunliffe WJ. Disorders of sebaceous glands. In: Burns T, Breathnach S, Cox N, Griffith C, editors. Rook's textbook of dermatology. 7th ed. Massachusetts, USA: Blackwell Publishing Company; 2004. p. 43.1-43.78.

- 2. Collier CN, Harper CJ, Cantrell WC. The prevalence of acne in adults 20 years and older. *J Am Acad Dermatol* 2007;58:56–9.
- Al-Shobaili HA, Salem TA, Alzolibani AA, Robaee AA, Settin AA. Tumor necrosis factor-a -308 G/A and interleukin 10 -1082 A/G gene polymorphisms in patients with acne vulgaris. *J Dermatol Sci* 2012;68:52-5.
- 4. Suh DH, Kwon HH. What's new in the physiopathology of acne? Br J Dermatol 2015;172 Suppl 1:13-9.
- Papakonstantinou E, Aletras AJ, Glass E, Tsogas P, Dionyssopoulos A, Adjaye J, et al. Matrix metalloproteinases of epithelial origin in facial sebum of patients with acne and their regulation by isotretinoin. J Invest Dermatol 2005;125:673–84.
- Melnik Bodo C. Acneigenic stimuli converge in phosphoinositol-3 kinase/ Akt/Foxo1 signal transduction. *J Clin Exp Dermatol* 2010:1–8.
- Chen WC, Zouboulis CC. Hormones and the pilosebaceous unit. Dermatoendocrinology. 2009;1:81-86.
- Chen W, Thiboutot D, Zouboulis CC. Cutaneous androgen metabolism: Basic research and clinical perspectives. *J Invest Dermatol*. 2002;119:992–1007.
- Thiboutot D, Harris G, Iles V. Activity of the type 1 5 alpha-reductase exhibits regional differences in isolated sebaceous glands and whole skin. J Invest Dermatol 1995;105:209–14.
- Kanda N, Watanabe S. 17β-estradiol inhibits the production of interferon-induced protein of 10 kDa by human keratinocytes. *J Invest Dermatol* 2003;120:411–9.
- 11. Kumari R, Thappa DM. Role of insulin resistance and diet in acne. *Indian J Dermatol Venereol Leprol*. 2013;79:291-9.
- 12. Chuan SS¹, Chang RJ. Polycystic ovary syndrome and acne. Skin Therapy Lett. 2010 Nov-Dec;15(10):1-4
- Schuster M¹, Zouboulis CC, Ochsendorf F, Müller J, Thaçi D, Bernd A, Kaufmann R, Kippenberger S. Peroxisome proliferator-activated receptor activators protect sebocytes from apoptosis: a new treatment modality for acne? *Br J Dermatol*. 2011 Jan;164(1):182-6.
- Dozsa A^{1,2,3}, Mihaly J¹, Dezso B⁴, Csizmadia E¹, Keresztessy T³, Marko L³, Rühl R¹, Remenyik E³, Nagy L^{1,5}.Decreased peroxisome proliferator-activated receptor γ level and signalling in sebaceous glands of patients with acne vulgaris. *Clin Exp Dermatol.* 2016 Jul;41(5):547-51.
- 15. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985 Jul;28(7):412-9. PMID:
- Tsai MC¹, Chen W, Cheng YW, Wang CY, Chen GY, Hsu TJ. Higher body mass index is a significant risk factor for acne formation in schoolchildren. *Eur J Dermatol.* 2006 May-Jun;16(3):251-3.
- Halvorsen JA, Vleugels RA, Bjertness E, Lien L.A population-based study of acne and body mass index in adolescents. *Arch Dermatol.* 2012 Jan;148(1):131-2. doi: 10.1001/archderm.148.1.131
- Lu PH^{1,2}, Hsu CH, Body mass index is negatively associated with acne lesion counts in Taiwanese women with post-adolescent acne. *J Eur Acad Dermatol Venereol.* 2015 Oct;29(10):2046-50. doi: 10.1111/jdv.12754. Epub 2014 Sep 30.
- A Hatwal, SK Singh, JK Agarwal, G Singh, HS Bajpai, SS Gupta, Serum testosterone, DHEA-S and androstenedione levels in acne, Year : 1990 | Volume : 56

| Issue : 6 | Page : 427-429 indian journal of dermatology, venereology and leprology.

- Yang XQ, Shen XL, Wu ER, Xia T Testosterone and estradiol serum levels in acne. A *Chin Med J (Engl)*. 1989 Mar;102(3):236-8.
- Nazan Emiroğlu,¹ Fatma Pelin Cengiz,¹ and Funda Kemeriz, Insulin resistance in severe acne vulgaris, Postepy Dermatol Alergol. 2015 Aug; 32(4): 281–285.
- 22. Michela Del Prete, Maria Chiara Mauriello, Insulin resistance and acne: a new risk factor for men? Endocrine (2012) 42:555–560.
- Prathima Munichandrappa*, Manjunath K. G., Kiran C., Anirudh Variyar, A comparative study of insulin resistance in acne vulgaris, *Int J Res Dermatol*. 2017 Sep;3(3):403-406
- 24. Shibata M, Katsuyama M, Onodera T, Ehama R, Hosoi J, Tagami H. Glucocorticoids enhance Toll-Like Receptor 2 expression in human keratinocytes stimulated with Propionibacterium acnes or proinflammatory cytokines. J Invest Dermatol 2009;129:375–82.
- Scholzen TE, Brzoska T, Kalden DH. Expression of functional melanocortin receptors and proopiomelanocortin peptides by human dermal microvascular endothelial cells. Ann N Y Acad Sci 1999;885:239–53.
- 26. Ola Ahmed Bakry, Rania Mohamed Azmy El Shazly,¹ Shawky Mahmoud El Farargy, and Dalia Kotb. Role of hormones and blood lipids in the pathogenesis of acne vulgaris in non-obese, non-hirsute females. *Indian Dermatol Online J.* 2014 Nov;5(Suppl 1):S9–S16.
- Iurassich S¹, Trotta C, Palagiano A, Pace L. [Correlations between acne and polycystic ovary. A study of 60 cases]. Minerva Ginecol. 2001 Apr;53(2):107-11.
- Sayera Begum*, M Zakir Hossain**, Md. Fashiur Rahman†, Laila Anjuman Banu‡ Polycystic ovarian syndrome in women with acne *Journal of Pakistan* Association of Dermatologists 2012;22:24-29.