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Research Article

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A Study on Correlation Between Serum Free Testosterone Levels And Adult Acne In Women at A Tertiary Care Hospital

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ABSTRACT

Background: Acne is generally regarded as a skin disorder of adolescents, but off late the prevalence has been increasing in adults too; especially in women. Hyperandrogenism is considered as an important contributing factor for the development of acne in adult women. If elevated androgens are found patients may benefit from various methods of hormonal therapy and reduce psychological morbidity. As there is paucity of data on role of circulating androgens in female acne, this study was undertaken to evaluate the same.
Aims and objectives: To evaluate the correlation between serum free testosterone levels and adult acne in females.
Materials and methods: A case control study from January 2020 to June 2021 was conducted at Department of DVL, Guntur Medical College. 50 adult acne female patients and 50 age and sex-matched healthy controls were enrolled in the study. Blood levels of free testosterone, total testosterone, sex hormone binding globulin were measured on day 1-3 of menstrual cycle and free androgen index was calculated.
Results: Adult acne cases were commonly reported in 25-30years age group with moderate severity. Although free testosterone levels were within normal limits in cases statistically significant difference was seen compared to the controls. Total testosterone and free androgen index vales were significantly elevated in cases and correlated positively with severity of acne.
Conclusion: Free androgen index can be used as a surrogate marker for hyperandrogenemia in cases where free and total testosterone cases fall within normal limits. We reiterate the role of androgens and as a corollary the need for hormonal evaluation and timely anti- androgen therapy for adult acne in females.

Key Words: *Adult acne, Androgens, Free testosterone, Free androgen index.*

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INTRODUCTION:

Adult acne predominantly seen in females, is defined as the presence of acne beyond theage of 25 years [1–3] and it is of two subtypes:

Persistent acne: continues from adolescence into adulthood; commonly seen subtype [4–6]Late-onset acne: appears for the first time beyond 25 years of age [7,8].

In addition to these there is a third type called recurrent acne which persists fromadolescence improves for a variable time but recurs back in adulthood[9].

Acne lesions in adult females are observed to be localized more in lower third of face including mandible, chin, perioral and anterior cervical region. Lesions are predominantly inflammatory and increased seborrhea may not be seen in all cases except for the ones withmore of open comedones and microcysts.

Acne is a multi factorial disorder and some important steps in pathogenesis are 1) abnormal hyper keratinization of infundibular epithelium and obstruction of sebaceous follicles 2)androgenic stimulation of the sebaceous glands 3)microbial colonization of pilosebaceousunits by Cutibacterium acnes and subsequent perifollicular inflammation[10,11] 4) genetic predisposition

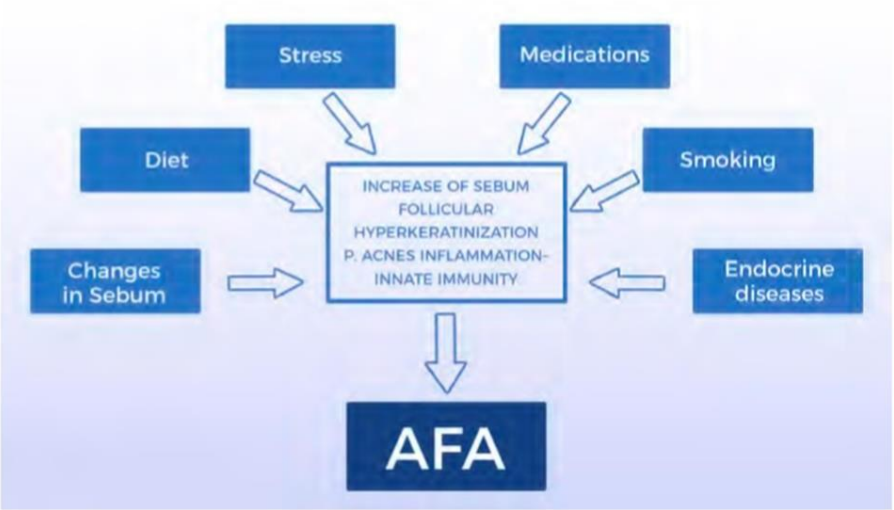

Figure 1 interplay of causative factors in adult female acne(12)

The role of testosterone in adult female acne best explained as follows-

I. Increased end organ sensitivity: sebocytes and keratinocytes of adult acne patients possess increased number and more sensitive receptors to circulating androgens[13]
II. Increased peripheral metabolism of androgens
III. Increased or abnormal activity of enzymes concerned with androgen metabolism

Excess of androgens whether consequent to ovarian or adrenal pathology is one of the most commonly encountered endocrine dysfunction in adult female acne[14]. Hence it is important to investigate a thorough hormonal profile in adult acne patients and this study was taken up to see the amount of correlation.

MATERIALS AND METHODS:

Source of data:

The study was conducted in the Department of Dermatology, Venereology and Leprology; Guntur medical college, Government general hospital, Guntur, Andhra Pradesh. 50 adult female patients with acne and 50 age and sex-matched healthy controls were enrolled in the study from January 2020 to June 2021 (18months).

Method of data collection:

Informed written consent was taken from the study participants. A pre-structured proforma was used to collect detail history and dermatological examination was done. Blood investigations were done on day 1-3 of menstrual cycle for free and total testosterone and sex hormone binding globulin. Free androgen index was calculated using the formula- FAI= TT x 100/SHBG (nmol/L). levels more than 5 was considered abnormal. The values were compared with control group and possible correlation with severity of acne among cases was sought out. Clinical grading was done using GAGS score.

Inclusion criteria:

Females with acne aged ≥25 years attending dermatology opd willing to undergo study were taken.

Exclusion criteria:

Females with conditions known to have hyperandrogenism like congenital adrenal hyperplasia, PCOS and androgen secreting tumours.

Patients receiving treatment with isotretinoin, oral contraceptives, anti-androgens or systemic antibiotics for three months prior to the study.

STATISTICAL ANALYSIS:

The data was put into tables and analysed using standard statistical methods like Percentages, Proportions, Independent samples 't' test, Mann-Whitney U test. Correlation between severity of acne and free, total testosterone and free androgen index was calculated using Pearson's correlation coefficient. In all the tests mentioned above, a "p" value of less than 0.05 was considered to be statistically significant. All the statistical calculations were performed using IBM SPSS 20.0. Pearson's correlation coefficient was calculated using Pearson's Rho calculator. Microsoft Word and Excel were used for preparation of graphs and charts.

RESULTS:

Majority (62%) of the cases belonged to <30 years of age group, whereas 34% and 4% belong to the age group of 31-40 and 41-40years of age group respectively. Meanage and standard deviation of cases was 30.28±4.91 years. Mean age and SD of controls was 34.94±5.11 years. Out of 50 acne cases in this study 52% (26) of them had persisting type of adult acne and the remaining 48% (24) had new adult-onset acne. It has been observed that 33 of the cases were overweight with BMI between 25-29.9 kg/m^2.

The cases were graded based on their severity using Global Acne Grading Systemscore. Out of 50 cases 48% (24) had moderate degree of acne, 40% (20) had milddegree of acne, 8% (4) had severe grade of acne and only 4% (2) had very severe grade of acne.

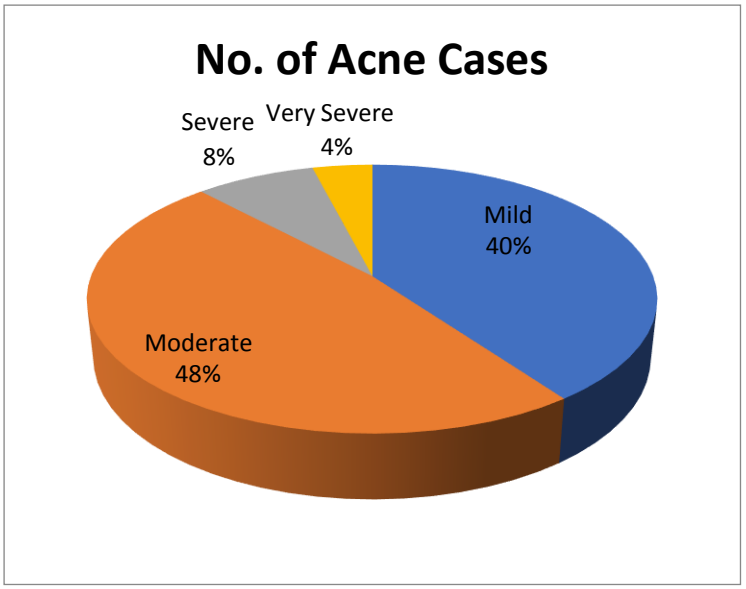

Figure 2 Grading of acne severity

TABLE 1: COMPARSION OF FREE TESTOSTERONE (FT) LEVELS BETWEEN CASES AND CONTROLS:

Variables	Cases		Control		P value
	Mean	SD	Mean	SD	
FT	0.45	0.24	0.37	0.17	0.04

Independent samples t-test.

Variables	Cases		Control		P value
	Median	IQR	Median	IQR	
FT	0.43	0.39	0.37	0.27	0.001

Mann-Whitney U test

The median Free Testosterone (FT) were statistically significant, with a p-value of 0.001(<0.05 being significant) calculated using the Independent samples t-test indicating FT values in both groups were comparable with a significant difference.

TABLE 2: COMPARSION BETWEEN CASES AND CONTROLS BASED ON TOTAL TESTOSTERONE VALUES:

Variables	Cases		Control		P value
	Mean	SD	Mean	SD	

TT	**10.62**	**5.64**	**4.67**	**2.06**	**0.001**

Independent samples t-test.

The mean total testosterone values for cases was 10.62 and 4.67 among controls whichshowed a statistically significant difference (p-value=0.001).

TABLE 3: COMPARSION OF SEX HORMONE BINDING GLOBULIN (SHBG) VALUES BETWEEN CASES AND CONTROLS:

Variables	**Cases**		**Control**		**P value**
	Mean	**SD**	**Mean**	**SD**	
SHBG	**87.38**	**21.88**	**107.33**	**14.58**	**0.002**

Independent samples t-test.

The mean SHBG value is 87.38 for cases and 107.33 for controls and results are statisticallysignificant with a p-value of 0.002.

TABLE 4: COMPARSION OF FREE ANDROGEN INDEX VALUES BETWEEN CASES AND CONTROLS:

Variables	**Cases**		**Control**		**P value**
	Mean	**SD**	**Mean**	**SD**	
FAI	**14.17**	**10.75**	**4.25**	**1.79**	**0.01**

Independent samples t-test.

The results are statistically significant for FAI as p-value obtained is 0.01.

CORRELATION BETWEEN SEVERITY OF ACNE AND Free Testosterone (FT)

The calculated value of Pearson Correlation for correlation between acne severity and FreeTestosterone was r = + 0.52 with a p (2 tailed) value = 0.0001 (p value < 0.05 being significant).There was highly significant correlation between acne severity and Free Testosterone of cases in the present study.

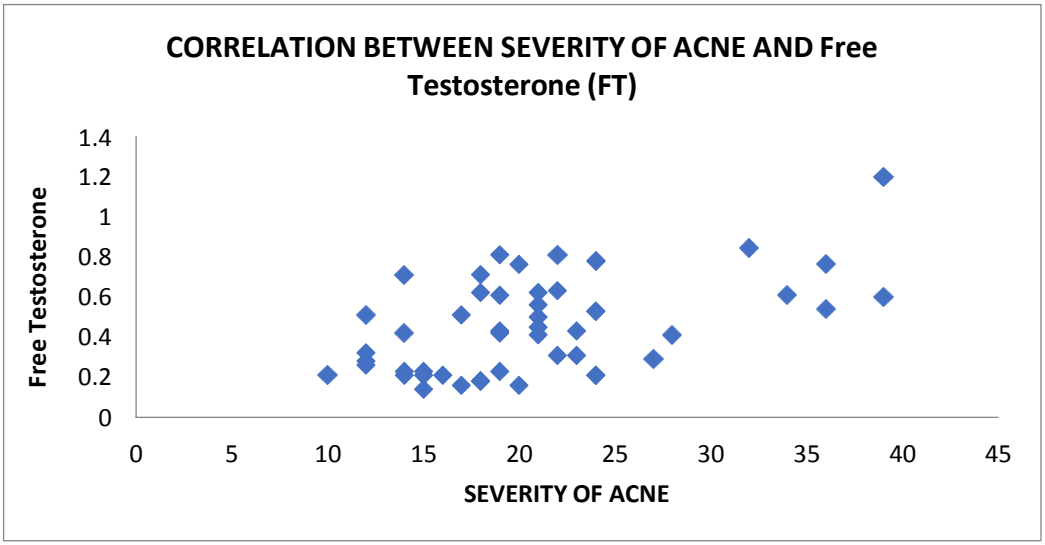

Figure 3 scatterplot of acne severity and free testosterone

CORRELATION BETWEEN SEVERITY OF ACNE AND Total Testosterone (TT)

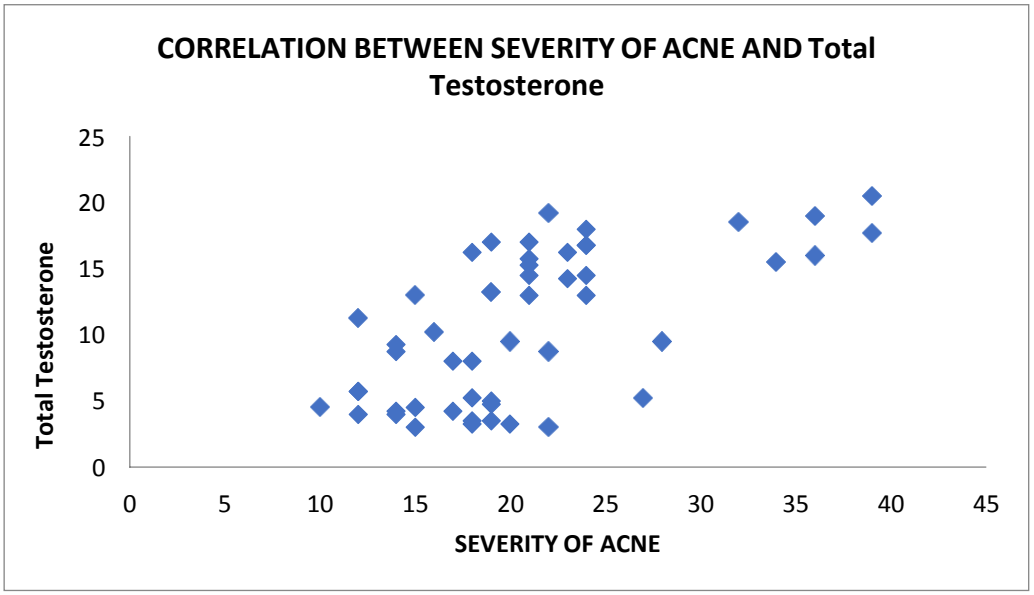

Figure 4 scatterplot of total testosterone and acne severity

The calculated value of Pearson Correlation for correlation between acne severity and TotalTestosterone (TT) was r = + 0.632 with a p (2 tailed) value = 0.0002 (p value < 0.05 being significant).There was highly significant correlation between acne lesions severity and TotalTestosterone (TT) of cases in the present study.

CORRELATION BETWEEN SEVERITY OF ACNE AND Free Androgen Index (FAI)

The calculated value of Pearson Correlation for correlation between acne severity and Free Androgen Index (FAI) was r = + 0.764 with a p (2 tailed) value = 0.0001 (p value < 0.05 being significant).There was highly significant correlation between the severity of acne lesions and Free Androgen Index (FAI) of cases in the present study.

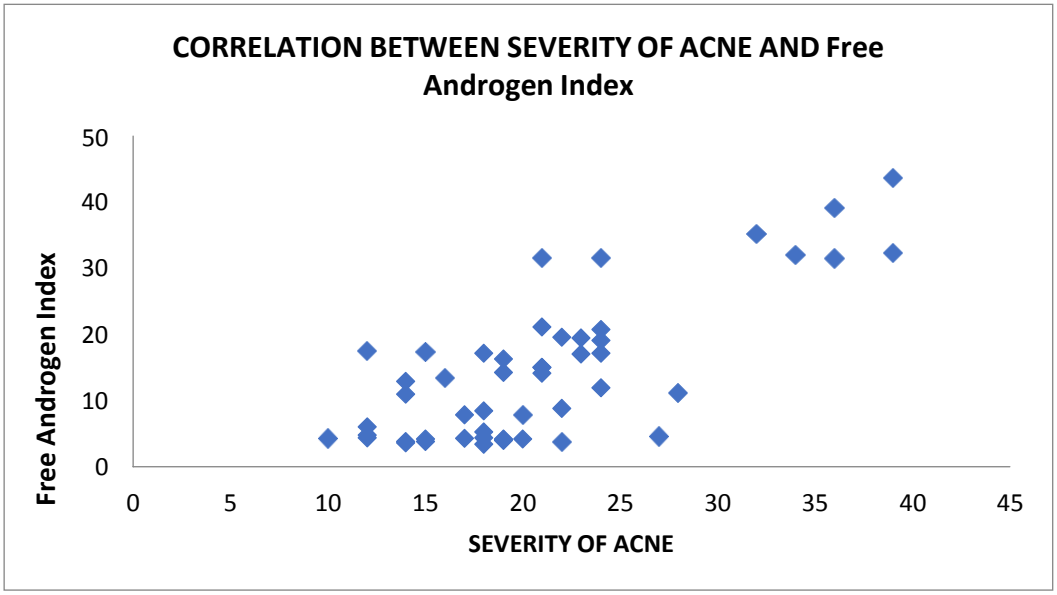

Figure 5 scatterplot of free androgen index and acne severity

DISCUSSION:

Acne is a disorder of the pilosebaceous unit, and its considered as a commonly encountered skin condition among adolescent age groups. However, it has been shown that acne can persist into adulthood or even begin later on after 25 years of age. Androgens are an essential prerequisite for the pathogenesis of acne. Acne is a common sign of hyperandrogenemia. It is of paramount importance to identify causative factor in order to give targeted therapy and avoid any systemic and reproductive consequences in females. Asit is generally considered that the non-protein-bound fraction is available to the tissues, freetestosterone has been considered as a marker for biologically available testosterone[15] .In the current study the significance of free testosterone as a precursor androgen in development of acne, which was

indicated by Lucky et al[16] was confirmed.

In the present study where 50 adult acne cases were studied 52 % (n=26) of them presented with persisting type of adult acne, and 48% (n=24) were having late-onset adult acne. In another similar study done by Khunger et al[17] 73.2% (n=205) of the cases were having persistent type of adult acne and 26.8% (n=75) of the cases presented with late-onset adult acne. In a study conducted by Bansal et al[2] out of 165 cases 56% (n=94) had late-onset acne and 43% (n=71) of the cases had persisting type of adult acne.

Our study findings were concurrent with that of Khunger et al [17] where both studies found majority of the cases having persisting type of adult acne. Bansal et al[2] study findings were contrary to our observation, they found most of the patients having late-onsettype of adult acne.

In our present study, out of the 50 acne cases, 40% (n=20) had mild acne, 48% (n=24) had moderate acne, 8% (n=4) had severe and 4% (n=2) had very severe acne. Bansal et al[2] conducted a similar study on adult female acne, out of 165 cases 79.17% had mild acne and20.83% had moderate acne with a mean GAGS of 15.57±4.04.

In our study we have found that median values of free testosterone of cases and controls were statistically significant with a p-value of 0.001 (<0.005 being significant). We observed the mean value of free testosterone was 0.45pg/ml for cases with a standard deviation of 0.24; whereas the controls had a mean value of 0.37pg/ml with a standard deviation of 0.1.The results obtained had a statistically significant difference with a p-value=0.04. The highest value was 1.20 pg/mL in cases and 0.71 for controls; whereas the least value was 0.14pg/ml in cases and 0.09pg/mL in controls. Although our study population had FT values within normal range there was significant difference when compared between cases and controls.

Schiavone et al[15] conducted a similar study with 24 age and gender matched cases and controls in Atlanta. They observed mean FT value of 1.035 ng/dL with a standard deviation of 0.49 in cases; whereas controls had a mean value of 0.54 ng/Dl with a standard deviationof 0.25, they found significant difference with a p-value=0.01.

Slayden et al(18)conducted a similar study in Mexico and found median value of 18 pmol/L for cases and 13.2 pmol/L for controls with a statistically significant difference as p- value=0.01.Aizawa et al(19) has done a similar study in Tokyo and adrenal androgen abnormalities in women with late onset and persistent acne and he found free testosterone values were significantly higher in cases than controls with a p-value<0.001.

In another similar study conducted by Lucky et al.[16] they similarly found significant difference in free testosterone values with a p-value<0.002.Our study results are in accordance with the results obtained by previous studies conducted by Schiavone et al.[15],Slayden et al.[20] , Aizawa et al.[19] & Lucky et al.[16]

In our study FAI values varied between cases and controls. The mean value for cases was 14.17 with a standard deviation of 10.75, whereas the controls had a mean value of 4.25 with standard deviation of 1.79. The results obtained were statistically significant as p-valueis 0.01.

Seirafi et al[10] in a study in Iran on androgens in women with adult-onset acne found lower levels of SHBG, and higher levels of FAI in patients with acne than control groups. The results obtained were statistically significant as p-value was 0.02.

Bansal et al[2] in a prospective study on hormonal abnormalities in adult female acne found that FAI was elevated in 15.83% out of 120 study population. They found SHBG mean value was relatively low with a mean value of 53.61 and standard deviation of 44.35 similar to our results. Free androgen index was calculated as a surrogate marker of hyperandrogenemia aswe observed cases with normal free and total testosterone values also had raised FAI.

CONCLUSION:

In our study adult female acne cases were more commonly reported in 25-30 years age group. Moderate grade of acne cases were commonly seen. Although free testosterone values were within normal limits in cases there was statistically significant difference when compared with controls without acne. Raised total testosterone values and decreased sex hormone binding globulin values observed in acne cases compared to controls resulted in increased free androgen index for cases. Free and total testosterone and free androgen index values correlated positively with the severity of acne, which need to be studied more extensively in a larger population. Free androgen index can be used as a surrogate marker for hyperandrogenaemia in cases where free and total testosterone cases fall within normal limits. We reiterate the role of androgens and as a corollary the need for hormonal evaluation and timely anti-androgen therapy in adult female acne.

ETHICAL APPROVAL: Approval for the study was obtained from Institutional Ethics Committee, Guntur Medical College, AP, India

CONSENT: Written and informed consent was obtained from all participants of the study.

LIST OF ABBREVIATIONS: FT-Free testosterone, TT-Total testosterone, SHBG-Sex hormone binding globulin, FAI-Freeandrogen index

DATA AVAILABILITY: Data related to the study is available is available upon request from the correspondingauthor.

CONFLICTS OF INTEREST: None declared

FUNDING STATEMENT: No financial support.

AUTHORS CONTRIBUTION: SG collected, interpreted and prepared the manuscript. MR guided and supervised at all stages. DSS helped with methodology and final manuscript. All authors read and approvedthe final manuscript.

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