ORIGINAL ARTICLES

Association of Serum Testosterone with Acne Vulgaris in Women

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Abstract:

Background: Androgens enhance the sebum production and follicular keratosis that plays the key role in the aetiology of acne. **Objective:** To find out the association between serum testosterone and acne vulgaris. **Methods:** A case control study was carried out for a period of two years in the outpatient department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Female patients having acne vulgaris were selected as case. Healthy control (age and sex matched) were enrolled from the community. **Results:** The study showed that the mean age of the cases was 22.43 with standard deviation 5.2 years and the mean age of the control was 23.23 with standard deviation 5.9 years. The mean duration of disease was 62.6 months ranging from 12 months to 300 months. All the patients had presented with comedones (blackheads and whiteheads) followed by 94.3% had papules and 58.6% had pustules. Considering the site of lesion, all the patients had acne in the face. Data analysis revealed that the percentage of serum testosterone above normal was found to be high among the cases with acne (10%) whereas below normal level of serum testosterone was found among the control and the difference was statistically significant (p<0.001). **Conclusion:**The study found a significant association between serum testosterone and acne vulgaris. As serum testosterone is associated with acne vulgaris, testosterone levels should be measured in patients presenting with acne vulgaris especially in treatment resistant cases and anti-androgen treatment may be indicated in cases with elevated testosterone level.

Key words: Serum testosterone, acne vulgaris.

Introduction:

Acne is the most common disease of the skin.[1] Acne vulgaris is a self limited disease that affects the sebaceous follicles. [2] Acne vulgaris, depending on definition, affects 20-90% of all adolescents, with spontaneous resolution, in most cases, in late teens or early twenties.[3] Acne is a multifactorial disorder. Some important pathogenic factors involved include hyperkeratinization and obstruction of the sebaceous follicles as a result of abnormal keratinization of the infundibular epithelium, androgenic stimulation of the sebaceous glands and microbial colonization of the pilosebaceous units by Propionibacterium acnes and subsequent perifollicular inflammation.[2]

It occurs predominantly on the face and to a lesser extent, on the neck, back and chest.[1] Androgens (Total testosterone, androstenedione, dehydroepiandrosterone sulphate) are involved in the development of acne.[4] The skin is a typical target tissue for androgens and testosterone, a major androgen in human blood that stimulates many metabolic processes in the endothelium of sebaceous gland.[5] Raised androgen levels (testosterone, androstenedione, dehydroepiandrosterone, dehydroepi-androsterone sulphate) in women with acne have been repeatedly demonstrated in many studies. Androgens enhance the sebum production and follicular keratosis that plays the key role in the aetiology of acne.[6] Acne is a common feature in the course of endocrine diseases, characterized by raised levels of androgens.[3] The mechanisms suggested include: Increased circulating levels of androgens, increased local metabolism of androgens in skin and increased tissue sensitivity to androgens.[7]

Acne and hirsutism are common manifestations of hyper androgenism. Nevertheless, acne or hirsutism may be

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found with normal androgenic parameters. Increased sensitivity of sebaceous end organ to androgen and increased peripheral metabolism of androgen are other possible mechanisms involved in the development of acne.[2] As there is inadequate evidence on the status of circulating testosterone in patients of acne, this study is undertaken for evaluation. Serum testosterone level estimation is a simple cost effective laboratory test that could give us a clue of disease status. If elevated levels are found, specific antiandrogen treatment can be highly successful in the management of the disease. To the best of my knowledge there is no previous study of estimation of serum testosterone in patients with acne vulgaris in women in Bangladesh. A conclusive result will be of benefit to patients with acne in our country.

Methods:

It was a case control study. The study was carried out for a period of 2 years from March 2009 to February 2011, in the outpatient department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Female patients having acne vulgaris were selected as study population. Healthy control (age and sex matched) were enrolled from the community. Seventy patients were considered as Group A- case (Acne female patients), and seventy patients were considered as Group B- control (Normal female). Purposive type of non-probability sampling technique was followed. Data were recorded on pre designed data collection sheet. Within the period of data collection, patients were assigned purposively considering exclusion and inclusion criteria of patient selection.

Selection criteria:

Inclusion criteria for case: Patients having clinically diagnosed acne vulgaris. (Seborrhea i.e. greasy skin, comedones, papules, pustules, nodules and scarring, in some cases, predominantly on the face and to a lesser extent on the back and chest.)

i. Female patients of age 13 to 45 years.

ii. Patients willing to participate in this study.

Exclusion criteria for case: Patients not willing to participate.

i. Pregnant women and lactating mothers.

ii. Patients treated with oral contraceptive pill, antiandrogen, systemic antibiotics and oral retinoids within 3 months prior to the study.

iii. Patients treated with topical medication such as antibiotics, benzoyl peroxide, tretinoin, adapalene, tazarotene within 1 month prior to the study.

iv. Women on medication known to affect androgen action or metabolism such as oestrogen, dilantin, cimetidine, spironolactone, cyproterone acetate, corticosteroid, finasteride.

Inclusion criteria for control: Age and sex matched eumenorrhoeic healthy female.

ii. Individuals willing to participate in this study.

Exclusion criteria for control:

1. Not willing to participate

2. Individuals on hormonal contraceptives.

Study procedure:

Clinically suspected cases of acne vulgaris attending in the out patient Department of Dermatology and Venereology, BSMMU, Dhaka were seen. All women participating in the study gave informed consent. According to a structured questionnaire their particulars and history were taken. Patients for the study were selected on the basis of history, clinical examination and inclusion and exclusion criterias. Acne vulgaris was diagnosed by seborrhea (greasy skin), comedones, papules, pustules, nodules and scarring, in some cases, predominantly on the face and to a lesser extent on the back and chest.

Acne was graded according to the Consensus Conference on Acne Classification convened by American Academy of Dermatology in Washington DC on march 24 and 25, 1990 (Slayden et al. 2001). According to these criteria, mild acne is defined by the presence of comedones, without significant inflammation and a few or no papules; moderate acne, by the presence of comedones, with marked inflammatory papules and pustules and severe acne, by the presence of inflammatory nodules, in addition to comedones, papules and pustules.

Then from the selected patients blood samples were collected with aseptic measures for estimation of serum total testosterone.

Sample collection and preservation: After informed consent, all patients and control women were subjected to the same experimental protocol. Serum sample were drawn during the luteal phase (between 18th and 25th days of the menstrual cycle). With all aseptic precautions 3 ml of blood was collected from the median antecubital vein by disposable plastic syringe. The needle was detached from the nozzle and blood was transferred immediately into a dry, clean plastic test tube with a gentle push to avoid haemolysis. Collected blood was allowed to clot and then centrifuged. Separated serum was collected into plastic micro-centrifuged tubes and appropriately labeled and stored at -20°C until assayed.

Method of estimation: Microparticle Enzyme Immunoassay (MEIA) method (Newman 1999) by abbott, USA, AxSYM System auto analyzer. The method was used to determine serum total testosterone in the department of Biochemistry, BSMMU, Dhaka.

Ethical consideration: Prior to the commencement of this study, the research protocol was approved by the ethical review committee of BSMMU. The aims and objectives of the study along with its procedure, risk and benefits were explained to the patients in easily understandable local language and then informed consent was taken from each patient. It was assured that all information and records were kept confidential and the procedure would be helpful for both the dermatologists and the patients in making rational approach of the case management.

Data collection: Relevant data was collected in a preformed data collection sheet for each patient from the history, clinical examination and biochemical report. After collection, data was checked for inadequacy, irrelevancy and inconsistency. Irrelevant data was discarded.

Data processing and analysis: For the statistical analysis, one Microsoft Windows-based software package was used (SPSS [Statistical Package for Social Science] 15 for Windows, SPPS Incorporation, Chicago, IL, USA). Data process on categorical scale was presented as frequency and percentage and was analyzed by $\div^2$ test. While the data present on continuous scale was presented as mean and SD and analyzed with the help of Student's 't' test. Risk factor was analyzed. Statistical significance was set at 0.05 level and confidence interval at 95% level.

Results:

The study was carried out for a period of 2 years from outpatient department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Female patients having acne vulgaris were selected as study population. Healthy control (age and sex matched) were enrolled from the community. Seventy patients were considered as Group A- case (Acne female patients), and seventy patients were considered as Group B- control (Acne free female).

Table- I showed that the mean age of the cases was 22.43 with standard deviation 5.2 years and the mean age of the control was 23.23 with standard deviation 5.9 years and the main difference was not statistically significant (p > 0.05). Data showed that the highest percentage of patients were in the age group 20-24 years (41.4%) followed by less than 20 years (31.4%), 25-29 years (15.7%) and lowest in the age group 35 years and above (4.3%). Similar pattern of age structure was found in the control groups with highest percentage were in the age group 20-24 years (25.7%) followed by less than 20 years (24.3%) and equal percentage 25-29 years and 18.6% in the age group 30-34 years, p value reached from unpaired student's t test.

The mean duration of disease was 62.6 months ranging from 12 months to 300 months. It was found that 28.6% of the respondents had duration 12 to 24 months and equal percentage had 25-48 months. However, 27.1% of the patients mentioned that they were suffering from more than 6 years. All the patients had presented with comedones (blackheads and whiteheads) followed by 94.3% had papules and 58.6% had pustules. It was found that two fifths (40%) of the patients presented with mild acne and the 60% had moderate acne(Table-II).

Analysis revealed that mean serum testosterone was significantly high among the cases (0.52 ngm/ml) than the control (0.35 ngm/ml) and the mean difference was statistically significant (p<0.05). Data analysis revealed that the percentage of serum testosterone above normal was found to be high among the cases with acne (10%) whereas below normal level of serum testosterone was found among the control i.e. patients without acne and the difference was statistically significant (Table-III).

Table- I

Distribution of the patients by age, marital status, level of education and occupation (n=140)

Age in years	Case (n=70)		Control (n=70)		Total (n=140)		p value
	No.	%	No.	%	No.	%	
<20	22	31.4	17	24.3	39	27.9	
20-24	29	41.4	18	25.7	47	33.6	
25-29	11	15.7	17	24.3	28	20.0	
30-34	5	7.1	13	18.6	18	12.9	
>35	3	4.3	5	7.1	8	5.7	
Mean±SD (years)	22.43±5.2		23.23±5.9		22.83± 5.6		0.103*
Range (years)	15,40	15,40	15,40				

Case= Patients with acne vulgaris, Control= Females without acne vulgaris,

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Table-II

Distribution of the patients by duration of disease, pattern of skin lesion and its site

Duration of disease (Months)	Number	Percentage
12-24	20	28.6
25-48	20	28.6
49-72	11	15.7
e"73	19	27.1
Mean (SE)Range	62.57(6.4)12,300	
*Pattern of skin lesion		
Comedones	70	100.0
Papules	66	94.3
Pustules	41	58.6
Severity of acne		
Mild	28	40.0
Moderate	42	60.0

*Multiple responses

Table-III

Distribution of the study population by serum testosterone (n = 140)

Parameter	Case (n= 70)	Control (n= 70)	p value
Mean Serum Testosterone (ngm/ml)	0.52±0.02	0.35±0.02	p<0.001
Elevated	7	0	
Normal	63	57	0.001
Below normal	0	13	

Case= Patients with acne vulgaris, Control= Females without acne vulgaris, p value reached from t test.

Discussion:

This study was carried out in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, Dhaka. In this study, a total 140 females were enrolled with 70 having acne vulgaris considered as case and another 70 without acne vulgaris considered as control, to find out the association of serum total testosterone with acne vulgaris.

Age of the patients in this study ranged from 13 to 40 years. The mean age of the cases was 22.43 years with standard deviation 5.2 years. The mean age of the control was 23.23 years with standard deviation 5.9 years. Age of the control also ranged from 15 to 40 years. In a case control study by Slayden et al. ages of the women ranged from 12 to 43 years. Patients with acne and controls had similar mean (±SD) age (26.5±9.3 years vs. 29.2±4.7 years respectively).[1]

The mean duration of the disease in our study was 62.6 months (5.2 years) ranging from 12-300 months (1-25 years). It was found that 28.6% of the patients had duration 12-24 months and equal percentage had 25-48 months of illness and 27.1% of the patients were suffering from acne for more than 72 months. Zaenglein et al. 2008 found that in women acne persisted through the third decade or even later, which was consistent with this study.[8] In contrast to our study, Hatwal et al. found that the mean duration of acne was 2.6 years (range 1 to 6 years).[7] Borgia et al. 2004 reported mean duration of disease 5.9±4.6 years.[3] These results are similar to this study in respect of age incidence and duration.

In our study, 40% of patients had mild acne and 60% had moderate acne. In their case control study, Lookingbill et al. showed that mild acne was present in 44.44% of cases and moderate acne in 55.55% of cases.[9] These two findings were almost consistent with each other.

The current study revealed that serum testosterone was significantly high among the cases (0.52 ngm/ml) than the control 0.35 (ngm/ml) and the difference was statistically significant (p<0.05). There were many studies regarding correlation of acne and serum testosterone. Hatwal et al. found that, females with acne had significantly higher level of serum testosterone than controls.[7] Held et al. reported that, elevated serum testosterone levels were associated with acne and Darley et al. found increased testosterone or low SHBG (sex hormone binding globulin) alone or in combination in 60% of patients.[10,11] However, Levell et al. reported that acne was not associated with abnormal plasma androgens.[12] Zaenglein et al. 2008 stated that in the majority of acne patients serum androgens were within the normal range.[8] Cibula et al. demonstrated that, the severity of acne manifestation in adult women was not determined by androgen production and there must therefore be key factors other than androgen levels in the pathogenesis of acne.[6]

In our study we found elevated serum testosterone in 7 (10%) cases and below normal level of serum testosterone was found among 13 (18.6%) of the control individuals. The difference between case and control was statistically significant (p<0.001). Cibula et al. evaluated the relationship between acne severity and the clinical and laboratory markers of androgenicity in a large group of patients. Women examined consecutively in an out patient

unit for acne vlugaris over the years 1998-99 were included in the study. Inclusion criteria were age over 17 years, absence of hormonal therapy during the past 6 months and absence of therapy with systemic antibiotics or isotretinion at the time of examination. Patients with severe acne were not included as most women with this severity of acne did not meet the inclusion criteria of absence of systemic therapy. Ninety women over 17 years of age with acne were enrolled into the study. The patients were divided into three groups according to acne severity. Acne was graded using the Leeds technique as minor in 43(48%) cases, mild in 27 (30%) and moderate in 20 (22%). The level of testosterone were measured. The levels of at least one androgen were elevated over the reference value in 73 (81%) patients. Testosterone, DHEA, DHEAS and androstenedione levels were elevated in 22(24%), 17(19%), 27(30%) and 71(79%) patients respectively. In conclusion, their study did not demonstrate a positive correlation between androgen production and acne severity in a group of women over 17 years of age. While playing a part in acne development, enhanced androgen production does not have an effect on the degree of clinical manifestation of the disease. There must therefore be key factors other than androgen levels in the pathogenesis of severe acne. Their study suggests that the severity of acne manifestation in adult women is not determined by androgen production.[6]

Held et al. investigated the relationship between hyperandogenism and acne. Elevated serum androgen levels have been reported in patients with acne resistant to conventional dermatologic therapy. This study was designed to investigate the relationship between serum androgen levels and the presence of acne in an unselected population of women. Elevated serum testosterone levels were associated with acne vulgaris. Normal serum testosterone levels were found only in those patients with regular menstrual cycles.

Conclusion:
The study found a significant association between serum testosterone and acne vulgaris. As serum testosterone is associated with acne vulgaris, testosterone levels should be measured in patients presenting with acne vulgaris especially in treatment resistant cases and anti-androgen treatment may be indicated in cases with elevated testosterone level.

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