

Estimation of Serum Fasting Insulin in Patients with Acne Vulgaris and Compares these Values with that in Controls

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ABSTRACT

Introduction: Acne is a multifactorial inflammatory disease affecting the pilosebaceous follicles of the skin. Acne is a disorder resulting from the effect of hormones and other substances on the oil glands (sebaceous glands) and hair follicles present in the skin. The aim of this study was estimation of serum Fasting insulin in patients with acne vulgaris and compares these values with those in controls.

Methodology: This is the case control study which was carried out in the Departments of Biochemistry and Dermatology & Venereology of SGT Medical College Gurgaon. Fifty patients each of Mild (group I), Moderate (group II) and Severe Acne Vulgaris (group III) in age group 15-40 years were included as cases.

Result: In the present study, the level of serum insulin was significantly higher in moderate cases of acne as compared to controls. Therefore we suggest that insulin may also play an important marker for causing acne. Insulin stimulates the secretion of ovarian estrogen, androgen and progesterone which is consistent with our studies as increase in estrogen and testosterone has been also observed in moderate cases of acne.

Conclusion: Insulin was significantly higher in moderate cases as compared to controls. There by suggesting that insulin may play an important role to causation of acne.

Keywords: *Insulin, acne vulgaris, multifactorial inflammatory disease*

Introduction

Acne Vulgaris, chronic inflammatory dermatosis, insulin, hormonal misbalanced

Acne Vulgaris is a chronic inflammatory dermatosis notable for open or closed comedones (blackheads and whiteheads) and inflammatory lesions, including papules, pustules, or nodules (also known as cysts)¹.

The grading system of acne is based on the morphology of lesions. Acne was graded according to the Consensus Conference on Acne Classification convened by American Academy of Dermatology in Washington DC on 24-25 March, 1990².

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
- Severe acne, by the presence of inflammatory nodules, in addition to comedones, papules and pustules.

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The extra sebum or oil that is produced by the sebaceous glands mixes with dead skin cells and bacteria on the skin's surface and blocks these pores. Within the blocked pore, bacteria multiplies and cause inflammation. All of this leads to the lesions that are associated with acne. The pathophysiology of acne vulgaris can be broken up into four different events³:

1. Androgen-dependent overproduction of sebum
2. Follicular hyperkeratosis (closed and open comedones)
3. Increase in microbial flora (Propionibacteria acnes)
4. Immunological processes and inflammation

These events are not individual events, and are affected by each other. For example, the increase in proliferation of Propionibacteria acnes is a result of increased sebum production, as well as hyperkeratosis. However, the bacteria are responsible in part for producing factors such as bacterial lipases, proteases, hyaluronidases and chemotactic factors that stimulate inflammatory mechanisms. Follicular inflammation can also cause an increase in sebum production⁴.

The acne develops predominantly in adult age; possible reasons for this are diet, lifestyle and more synthetic hormones in our environment (foods, water, plastics and medication). By early recognition, the etiology and treatment protocol of acne may prevent unwanted conditions⁵. Since its first clinical description, acne has always been the subject of a great number of studies and research. But only very few of them dealt with the history of the disease focusing on semantic considerations. Therefore in the present work estimation of Fasting insulin in serum of patients with different grade of acne vulgaris patients will be analyzed and to compare with control groups.

Material & Method

This is the case control study which was carried out in the Departments of Biochemistry and Dermatology & Venereology of SGT Medical College Gurgaon. Fifty patients each of Mild (group I), Moderate (group II) and Severe Acne Vulgaris (group III) in age group 15-40 years were included as cases. All of them presented to the OPD of Departments of Dermatology & Venereology of SGT Medical College Gurgaon and students of SGT

University of varies faculty. A detailed history was taken and clinical examination was done. Fasting sample for estimation of all parameters was taken on second day of menstritation after the diagnosis was confirmed. Fifty healthy age matched females were recruited for the study as controls (group IV). Controls consisted of healthy volunteers. None of them had any prior history of medical disorders. Fasting sample was taken for the controls also. Duration of this study was one year (01/06/2015 to 31/05/2016). Institutional ethical committee clearance was also taken on 1/05/2015.

Selection of Cases: (Group I, II and III)

Inclusion criteria for group I: Fifty clinically diagnosed females were taken with Mild Acne Vulgaris, consists of open and closed comedones and some papules and pustules, based on detailed clinical history and examination.

Inclusion criteria for group II: Fifty clinically diagnosed females were taken with moderate Acne Vulgaris, consists of more frequent papules and pustules with mild scarring, based on detailed clinical history and examination.

Inclusion criteria for group III: Fifty clinically diagnosed females were taken with severe Acne Vulgaris, contains all of the above, plus nodules and abscesses and more scarring, based on detailed clinical history and examination.

Inclusion criteria for control group IV: Fifty healthy age matched females were taken as controls.

Exclusion criteria: (group I, II, III and IV)

- Patients on immunosuppressive therapy like corticosteroids, regular analgesic intake and hormonal therapy.
- Patients with concomitant inflammatory or autoimmune disease
- Patients with acute or chronic infections.
- Patients with acute or chronic inflammatory disorder.
- Patients with Acne other than Acne Vulgaris

Sample Collection and Storage: The samples were collected on the second day of menstrual cycle of the patient and before the start of treatment. Written and informed consent was taken from all subjects in the cases and control groups after explaining about the details of the study.

5ml venous fasting blood samples were taken from all the four groups of our study subjects in plain vacutainer under sterile conditions. Samples were centrifuged and separated immediately. Then serums were stored at -20° C till the time of analysis.

Estimation of Insulin

Reagents

- **Insulin Bead Pack:** Coated with monoclonal murine anti-insulin antibody.
- **Insulin Reagent Wedge:** Alkaline phosphatase (bovine calf intestine) conjugated to polyclonal sheep anti-insulin antibody and alkaline phosphatase (bovine calf intestine) conjugated to monoclonal murine anti-insulin antibody in buffer.
- **Insulin Adjustors:** Two vial (low and High), lyophilized insulin in a nonhuman serum matrix, with preservative. At least 30 minutes before use, reconstitute each vial by adding 4.0ml distilled or deionized water. Mix by gentle swirling or inversion.
- **Insulin Controls:** Two vials of lyophilized insulin in a nonhuman serum matrix, with preservative. At least 30 minutes before use, reconstitute each vial by adding 4.0 ml distilled or deionized water mix by gentle swirling or inversion.

Statistical Analysis: Data was collected and mean and SD for all the parameter was calculated. Statistical analysis was performed by the SPSS program for Windows, version 17.0.

Result

The Study Group: A cohort of Fifty female patients each of Mild (group I), Moderate (group II) and Severe Acne Vulgaris (group III) in age group 15-40 years, seen from 01/06/2015 to 31/05/2016 formed the study group.

The control group: Fifty healthy age matched females were recruited for the study as controls.

Table 1: Frequency of cases in Mild, Moderate, Severe and Control

Groups	Frequency	%
Control	50	25.0%
Cases	150	75.0%
Mild	50	25.0%
Moderate	50	25.0%
Severe	50	25.0%

In the present study, total 150 cases which were subdivided into mild 50 cases (25%), moderate 50 cases (25%) and severe Acne Vulgaris 50 cases (25%). The control group had 50 cases (25%). These values shows in Table 1.

Table 2: Frequency of age distribution in control, mild, moderate and severe cases

Age Groups	Control Frequency (%)	Cases			P Value
		Mild Frequency (%)	Moderate Frequency (%)	Severe Frequency (%)	
15-20 yrs	24 (48%)	30 (60%)	28 (56%)	16 (32%)	0.132
21-25 yrs	15 (30%)	8 (16%)	9 (18%)	14 (28.0%)	
26-30 yrs	6 (12%)	8 (16%)	11 (22%)	14 (28.0%)	
30-35 yrs	5 (10%)	4 (8%)	2 (4%)	6 (12.0%)	
Total	50 (100%)	50 (100%)	50 (100%)	50 (100%)	

Females in the age group of 15-35 years were included in this study. The distribution of age group in case and control is shown in Table 2 and Graph 2. The differences in age between cases and control was statistically not found to be significant (P =0.132)

Table 3: Comparison of age distribution in control and, mild, moderate and severe cases

Age	Control	Cases			P Value
	Mean ± SD	Mild Mean ± SD	Moderate Mean ± SD	Severe Mean ± SD	
Age	22.20 ± 4.94	22.78 ± 5.62	22.28 ± 4.77	23.86 ± 5.18	0.347

The mean age of control and cases (mild, moderate and severe acne) is as shown in Table-3 and Graph- 3. Differences in average age between cases and control was statistically not found to be significant (P =0.347)

Table 4: Correlation of age distribution in control and, mild, moderate and severe cases

		Mean Difference	Std. Error	p value
Control	Mild	-0.1	0.419	1.000
	Moderate	-0.98	0.546	0.381
	Severe	-5.200*	0.703	<0.001
Mild	Moderate	-0.88	0.57	0.555
	Severe	-5.100*	0.721	<0.001
Moderate	Severe	-4.220*	0.802	<0.001

There exist a significant correlation between control and severe, mild and severe and moderate and severe. (P value <0.001), thereby suggesting that cases of severe acne occur in older age group as compared to those with mild and moderate acne.

Table 5: Mean and Standard Deviation of the Insulin in Controls, Mild, Moderate and Severe Acne Vulgaris

		Control	Cases			P Value
			Mild	Moderate	Severe	
Insulin (µIU/mL)	Mean ± SD	15.63 ± 8.36	17.74 ± 7.67	20.11 ± 9.30	15.07 ± 7.85	0.017
	Median	16.25	17.00	22.20	13.86	
	Min - Max	2.01 - 34.50	4.60 - 30.50	3.30 - 38.30	3.03 - 36.38	

The value of insulin in cases and controls is as shown in Table13 and Graph 9. Insulin was found statistically significant lower (P=0.017) in control group as compared to cases of study group (mild, moderate and severe).

Table 6: Correlation of cases with each other and control in comparison to Insulin

		Mean Difference	Std. Error	p value
Control	Mild	-2.1044	1.60475	0.196
	Moderate	-4.4784	1.76845	0.016
	Severe	0.55944	1.62233	0.804
Mild	Moderate	-2.374	1.70487	0.226
	Severe	2.66384	1.55277	0.081
Moderate	Severe	5.03784*	1.72143	0.004

The difference of mean value of insulin was found to be significantly higher in moderate (P< 0.016) cases as compared to control and moderate with severe cases (P< 0.004). The mean values of serum insulin (fasting) were also found higher in mild acne (Mean ± SD 17.74 ± 7.67, P=0.196) as compared to controls (Mean ± SD 15.63 ± 8.36). However the difference was not found statistically significant (P= 0.196).

Discussion

Acne vulgaris is a common skin disease, affecting more than 85% of adolescents, women being affected

more frequently than men⁶. It is seen in nearly 100% of individuals at some time during their lives⁷. Although it does not affect overall health, its impact on emotional well-being and function can be critical, especially active acne and its sequel, like permanent scarring, leaves psychological stress that do not always correlate with the clinician’s assessment of severity at one point in time⁸⁻⁹. Our group Ist, IInd, and IIIrd comprised of patients of Mild, Moderate and Severe Acne Vulgaris. Group IV consisted of healthy controls.

The age of the patients ranged from 15 to 35 years with 50(100%) of mild acne, 50(100%) of moderate acne and 50(100%) of severe acne and 50(100%) of control healthy.

In the present study, acne seems to be mostly found in 15-20 years of age group i.e 41(82%) cases of mild acne, 35 (70%) cases of moderate acnes and 10 (20%) cases of severe acne whereas 33 (60%) cases of control group. Only 6 (12%) cases have severe acne between 31 to 35 years of age group. This fact can be appreciated in Graph 2. The severe acne was found significantly in higher age group as compared to mild and moderate acne¹⁰.

The mean values for age did not show significant variation in case when compared with control group and within the cases which is further supported by the work of Bassi et al ¹¹ Rahman et al ¹² and Rahman et al ¹³ who revealed that the mean values for age did not vary much in obese and non-obese females with acne vulgaris when compared with control group.

Insulin

In the present study, the level of serum insulin was significantly higher in moderate cases of acne as compared to controls. Therefore we suggest that insulin may also play an important marker for causing acne. Insulin stimulates the secretion of ovarian estrogen, androgen and progesterone which is consistent with our studies as increase in estrogen and testosterone has been also observed in moderate cases of acne.

The work of Emiroglu et al¹⁴ found that insulin resistance may have a role in the pathogenesis of acne and there exists a positive correlation between insulin resistance and severe acne vulgaris.

Shabir et al ¹⁵observed that the serum fasting insulin was elevated in index patients and their family members and found a heritable component of β -cell dysfunction in the families of women with PCOS, which is likely to be a significant factor for the predisposition of metabolic syndrome in these families.

Pace¹⁶ insisted that Insulin resistance has been found to be a major component of PCOS; interaction can occur whereby hyperinsulinemia can promote hyperandrogenism and possibly also vice-versa.

Conclusion

Acne Vulgaris is mainly diseases of adolescent age where as severe acne is likely to be found in higher age group.

Level of LH, estradiol, testosterone and insulin may be studied in cases resistant to conventional treatment of acne in women and in those with history and clinical features suggestive of PCOD or hyperandrogenism and in obese women with acne. Any hormonal imbalance found may be correlated to help management of such cases.

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