Role of Insulin Resistance in Acne Vulgaris: A Hospital Based Observational Study

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Background and aim: *This study was aimed to assess the role of insulin resistance in acne vulgaris.*
Materials and method: *This was a hospital-based, observational study done on 300outdoor patientswho were clinically diagnosed to have acne.HOMA IR (Homeostatic model assessment for insulin resistance) was calculated for all patients.*
Results: *In our study, out of 300 cases, 154 (51.3%) were females and 146(48.7%) were males. Most of the cases (29.6%) were between 16-20 years of age followed by (20.6%) 21-25 years of age. 72.7% of the patients were students. Out of 300, 54% patients were adopting high glycemic diet.Grade II acne was found in 182 of 60.7%, followed by grade III in 77 (25.7%); grade I in 26(8.7%) and grade IV in 15 (5%) patients.Fasting serum Insulin levels was raised(>20) in 48(16%) females and 38(12.7%) males.HOMA IR level was raised(>2.5) in 86(28.6%) patients out of which 48(55.8%) were females and 38(44.2%) were males. Out of 154 female patients 32 were positive for PCOS.*
Conclusion: *28.6% patients showed raised HOMA IR which shows that high glycemic diet plays a significant role in insulin resistance acne.*
Key words: *Acne vulgaris , Insulin resistance*

I. Introduction

Acne vulgaris is one of the most common inflammatory disorder of pilosebaceous unit characterized by comedones, papules, pustules and in severe cases presenting with nodules and pseudocysts. It is the most common disorder encounterd in day to day practice by dermatologists[1]. Although generally considered to be a benign, self limiting condition, but it may sometime cause severe psychological upset or disfiguring scars[2].

The greatest number of cases are seen in age group of 16-19 years in males and 14-17 years in females, after which the incidence steadily decreases. For most of the people, acne diminishes over time or decrease in severity after one reaches twenties. However, there's no way to predict how long time it will take to disappear entirely, some individuals will carry this condition into thirties, forties and beyond age groups.

In recent years multi-factorial nature of acne has been proposed[3]. The four major pathogenic factors implicated[4] are:-

- Increased sebum production
- Hypercornification of pilosebaceous duct
- Abnormal bacterial function
- Inflammation.

One of the important etiologic factor in acne is an increase in the sebaceous gland activity, which is androgen dependent.

Sebum production is one of the key factor in the pathogenesis of acne[5]. Sebum production is regulated by androgens and in few cases androgen excess may influence or aggravate acne in susceptible individuals[6,7]. Sebum production begins during puberty in correspondence with the peak levels of growth hormone and insulin like growth factor 1 (IGF- 1) that occur in mid puberty[8,9,10,11,12].

During puberty, there is also a transient decline in insulin sensitivity. Acne begins nearly same time as the gradual increase in plasma insulin level, pre adolescent increase in body mass index (BMI) and the increase in IGF-1 concentrations. Acne incidence corresponds more closely to the changing course of insulin and IGF-1 levels than it does to changes in plasma androgens. This is because insulin and IGF-1 levels peak during late

puberty and gradually decline until the third decade. Acne generally resolves by this time, although circulating androgens remain unchanged[12,13,14].

Most common cause of hyperandrogenemia in females is polycystic ovary syndrome (PCOS). PCOS usually manifests in the form of acne, hirsutism and menstrual irregularities[15]. Therefore, acne along with cosmetic concern, also a sign of underlying disease. PCOS is the most common endocrine disorder among women during their reproductive period. Insulin resistance is characterized by decreased cellular uptake of glucose and normal or increased serum levels of insulin.

In states of insulin resistance, the intracellular pool of the insulin-responsive glucose transporter 4 (GLUT4) is markedly reduced. GLUT4 proteins are stored in recycling endosomes until insulin stimulates the cell to deliver large numbers of recycling endosomes with GLUT4 to the plasma membrane to facilitate increased glucose uptake. However, in insulin-resistant states, higher than normal insulin levels are required to increase the membrane pool of GLUT4 for adequate glucose uptake.

Insulin resistance and resulting raised plasma levels of insulin both reported to be responsible for high androgen concentration by stimulating secretion of ovarian estrogen, androgen and progesterone. Insulin enhances androgen production by stimulating ovarian receptors of insulin and insulin-like growth factor[16,17]. Insulin is a mitogen when it binds to insulin receptor-A (IR-A) or IGF-1R. For its metabolic actions and in glucose metabolism, it binds to insulin receptor (IR-B). IGF-1 have been observed in adult women and men with acne, giving rise to the possibility of the role of GH, hyperinsulinemia, and IGF-1 in acne.

II. Materials and Methods

This was a hospital-based, observational study conducted in Department of Dermatology of Mahatma Gandhi Medical College & Hospital (MGMCH), Jaipur. A total of 300 outdoor, patients, clinically diagnosed to have acne were included in the study. All patients were investigated for their fasting blood sugar and fasting serum insulin levels .HOMA IR (Homeostatic model assessment for insulin resistance) was calculated for all patients. Patients with Diabetes mellitus , other metabolic disorders, pregnant and lactating females were excluded from the study. Ethical clearance was taken from the Ethics Committee, MGMCH, Jaipur.

III. Observations & Results

A total of 300 patients with acne vulgaris attending the Skin OPD of Mahatma Gandhi Medical College & Hospital, Jaipur were included in the study. One of their family members were interviewed. The age and sex distribution was as follows:

Table 1: Age wise distribution of the patients (N=300)

Age group	No of Patients	%
10-15	44	14.7
15-20	89	29.6
20-25	62	20.6
25-30	59	19.6
30-35	31	10.3
> 35	15	5
Grand Total	300	100.0

The age group wise distribution of the patients were as followed. The highest number of patients were 89 (29.6%) in between the age group 15-20, 62 (20.6%) patients in between the age group 20-25, 59 (19.6%) patients were in between the age group of 25-30 & 31 (10.3%) were present in between the age group 30-35. The least number of patients 15 (5%) were present inage group of above 35 years. The mean age of presentation was 20.9±6.1 years.

Table 2: Sex wise distribution of the patients (N=300)

Sex	No of Patients	%
Female	154	51.3
Male	146	48.7
Grand Total	300	100.0

Out of total 300 patients, Females were 154 (51.3%) and males were 146 (48.7%).

Table 3: Occupation wise distribution of patients

Profession	No of Patients	%
House Wife	22	7.3
Student	218	72.7
Workers	60	20.0
Grand Total	300	100.0

Out of total 300 patients, Maximum number of patients were found to be students 218 (72.7%); 60 (20%) were workers & 22 (7.3%) were house wife.

Table 4: Distribution of patients according to duration of acne (N=300)

Duration of acne	No of Patients	%
0-5 years	229	76.3
5-10 years	48	16.0
10-15 years	23	7.7
Grand Total	300	100.0

Table 5: Distribution of patients according to Personal Habits

Personal Habits	No of Patients	%
Alcohol	76	25.3
Smoking	66	22.0

Out of total 300 patients, 76 (25.3) were alcoholic; 66 (22%) were smokers.

Table 6: Distribution of patients according to their Diet

Diet	No of Patients	%
High glycemic	162	54.0
Low glycemic	138	46.0
Grand Total	300	100.0

162 (54%) patients were found to be having high glycemic diets; 138 (46%) were taking low glycemic diets.

Table 7: Distribution of patients according to Acne Grading

Acne Grading	No of Patients	%
I	26	8.7
II	182	60.7
III	77	25.7
IV	15	5.0
Grand Total	300	100.0

Grade II acne was found in maximum number of 182 (60.7%) patients; followed by grade III in 77 (25.7%) patients; then grade I in 26 (8.7%) and grade IV in 15 (5%) patients.

Table 8: Distribution of female patients having PCOS (N=154)

PCOS	No of Patients	%
Not Present	122	40.7
Present	32	10.7
Grand Total	154	51.3

Out of total 154 female patients; 32 were positive for PCOS.

Table 9: Distribution of patients according to Fasting Serum Insulin level

Serum Insulin level	Total Females-154		Total Males-146		Total	
	No	%	No	%	No	%
5-20	106	35.3	108	36.0	214	71.3
>20	48	16	38	12.7	86	28.7

Out of total 300 patents; 48 (16%) females and 38 (12.7%) males had raised fasting serum insulin levels i.e. (>20);Whereas 106(36%) male has normal fasting serum insulin level (5-20). The mean of fasting serum insulin level was 30.9±7.3.

Table 10: Distribution of patients according to HOMA IR

HOMA IR level	No of Patients	%
0.23-2.5	214	71.3
>2.5	86	28.7
Grand Total	300	100.0

Out of total 300 patients ; 86 (28.7%) patients were found to be having high levels of HOMA IR after mathematical calculation done by formula= HOMA-IR = [basal insulin (μU / mL x fasting glucose (mg/dL)] / 405 Normal range = 0.23 to 2.5 (average 0.99). The mean HOMA IR was found to be 2.7±1.5.

Table 11: Sex distribution of patients having raised HOMA IR

Sex	No of Patients	%
Female	48	55.8
Male	38	44.2
Total	86	100.0

Out of total 86 patients who had raised HOMA IR above the reference range; 48 (55.8) were females and 38 (44.2) were females.

Table 12: Distribution of patient taking high glycemic diet with Raised HOMA IR levels

Diet	No of Patients with raised HOMA IR level	%
High glycemic	64	74.4
Low glycemic	22	25.6
Grand Total	86	100.0

Out of total 86 patients who had high levels of HOMA IR; 64 (74.4%) patients were taking high glycemic diets.

Table 13: Distribution of patients who had raised Homo IR levels with acne group

Acne Grading	No of Patients	%
I	14	16.3
II	41	47.7
III	23	26.7
IV	8	9.3
Grand Total	86	100.0

Out of total 86 patients who had high levels of HOMA IR; Grade II was acne found in maximum number of 41 (47.7%) patients; followed by grade III in 23 (26.7%) patients; then grade I in 14 (16.3%) and grade IV in 8 (9.3%) patients.

IV. Discussion

Our study purpose was to investigate a possible correlation between acne vulgaris and insulin resistance in a sample size of 300 patients, who are in good general health, apart from their dermatological conditions. According to the inclusion criteria shown above, we decided to exclude patients who present with major metabolic disorders, diabetes mellitus pregnant and lactating women to avoid this bias.

The age group wise distribution of the patients were as followed. The highest number of patients 89 (29.6%) were in between the age group of 15-20 yrs and the least number of patients 15 (5%) were present in age group of above 35 years. The mean age of presentation was 20.9±6.1 years.(table 1)

In our study majority of the patients (29.6%) were between the age group of 15-20 years, similar results were observed in a community based study done by Smithard A et al. who noted maximum patients with acne between 14-16 years of age[18].

Goulden V et al. observed that in 7-17% of individuals clinical acne persists beyond the age of 25 years[19].

In our study we have observed that 34.9% of patients with acne were beyond the age group of 25 years which may be due to rising insulin level beyond the age of 25 years.

Slight female preponderance of 154 (51%) patients was seen in our study while remaining 146(48.7%) were males (Table 2).

Mahadevi Patil et al. studied 120 cases of acne vulgaris. Among 120 patients, 51 (42.5%) were males and 69 (57.5%) were females[20].

Duration of acne of 0-5 years was seen in 229(76.3%) patients out of total of 300 subjects, while 5-10 years of duration was found in only 48(16%) patients. A small percentage of 7.7% (23 patients) presented with duration of 10-15 years (Table 3).

Our study is in agreement with the study done by Mahadevi Patil et al. who found that 34(28.3%) patients had duration of lesions <1 year, 43 (35.9%) patients had duration between 1-2 years, 27 (22.5%) patients had duration of 3-4 years and 16 (13.3%) patients had duration more than 4 years[20]

High glycemic diet was seen in 54% (162) while remaining 46% (138) reported to have low glycemic diet (Table-6).

These results were consistent with the study done by Asli Aksu et al. who found that out of 50 acne patients and 36 control groups, glycemic index and glycemic load values were significantly higher in the acne vulgaris group than in the healthy control subjects ($p = .022$ and $p = .001$, respectively)[21].

Similar results were observed in various studies which suggested that high glycemic load (HGL) diets may trigger acne by inducing hyperinsulinemia and Low glycemic load (LGL) diets may play a dual role in improvement in acne severity and a parallel improvement in insulin sensitivity as well[22,23,24,28].

In our study, majority of patients 60.7% (182) demonstrated grade II acne followed by 25.7% (77) had grade III acne, 8.7% (26) had grade I acne and 5% (15) patients were observed to have grade IV acne (Table-7).

Data equivalent to our observations were reported by Seité S et al. who found that the most common acne grade was grade II in 70.7% patients, followed by grades I accounting for 21.5%, grade III accounting for 16.1%, and grade IV accounting for 5.8%[26].

Out of total 154 females, 106 (35.3%) had normal serum fasting insulin levels, the remaining 48 patients showed elevated levels (16%). Out of 146 male patients, 38 males had elevated level of serum insulin (12.7%) while remaining 108(36%) males demonstrated normal levels (Table-9) i.e. total of 28.7% patients showed elevated levels of serum fasting insulin.

Our observations correlates well with the study done by Michela del prete et al on 22 young males with acne and have found that the androgenic profile was normal, in all males with acne suggesting that acne in these patients can be influenced by hyperinsulinemia but not by androgen activity. This finding is supported by the fact that even in subjects with acne and BMI <24.9 there is an independent relationship between acne and hyperinsulinemia[27].

In our study, HOMA-IR index for evaluating insulin resistance was used. The HOMA-IR index has been an accepted formula for measuring insulin resistance since its original publication by Matthews et al. in 1985[27].

In our study we have found that 86(28.7%) patients were observed to have elevated values of more than 2.5 (cut of value), while 214(71.3%) patients showed normal values under 0.23-2.5 (Table-10).

A study by Michela Del Prete et al. was done by excluding subjects with overweight/obesity (BMI >24.9). 243 patients with severe acne vulgaris and 156 healthy controls were included. There was no difference between two groups in terms of weight, height or body mass index (all p values >0.05). While fasting blood glucose levels were not different between the groups (p > 0.05, 82.91 ±9.76 vs. 80.26 ±8.33), the fasting insulin levels were significantly higher in the patient group than in the control group (p < 0.001, 14.01±11.94 vs. 9.12 ±3.53).

Additionally, a highly significant difference between the patient and control groups in terms of HOMA values (p < 0.001, 2.87 ±2.56vs. 1.63 ±0.65)[28] were noted.

In our study out of 86 patients 55.8% (48) were females, and 44.2%(38) were males who showed elevated HOMA IR levels (Table-11).

We have found in our study that there's slight preponderance in female patients with acne who showed raised HOMA IR levels.

In the present acne study, acne grading of these 86 patients with raised HOMA IR values was done, and it was observed that majority of patients accounting for 47.7% (41) demonstrated grade II acne, 26.7%(23) showed grade III acne, 16.3%(14) showed grade I acne and 9.3%(8) patients were observed to have grade IV acne (Table-13).

V. Conclusion:

In our study we correlated acne grading with HOMA IR, it was observed that majority of patients 47.7% demonstrated grade II acne, followed by grade III, I and IV. Majority of patient with raised HOMA IR 74.4% was taking high glycemic diet which may play a significant role in insulin resistant acne.

We hereby conclude, that there is a strong need to evaluate patients on the basis of HOMA IR who are resistant to conventional treatment and of longer duration of acne vulgaris, for better diagnosis and treatment.

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