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Clinico-epidemiological profile of acne vulgaris and its relationship with insulin resistance in males vs females: A comparative study

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Abstract
Aim: To analyse the clinico-epidemiological profile of acne vulgaris and its relationship with insulin resistance among males and females.
Material and Method: The present cross sectional observational study was conducted in the department of Dermatology, Venereology and Leprosy at Chattrapati Shivaji Subharti Hospital from November 2018 to April 2020 for 1 and a half among 500 clinically diagnosed patients of acne vulgaris attending the out-patient department. General physical examination including BMI, anthropometry which includes height, weight, triceps skin thickness and waist/hip ratio was done. Investigations comprised of fasting blood sugar and fasting insulin levels. These assess the insulin resistance based on HOMA-IR.
Results: Out of 500 subjects, 262 (52.4%) were males and 238 (47.6%) were females. The mean age of the study group was 21.63 years. Males with BMI>25 kg/m^2 reported more acne vulgaris as compared to females with statistically significant difference. Overall, males underwent more stress than females. 53.84% of the patients consuming High Glycemic diet were males and rest females. Mean HOMA-IR was found more in grade IV acne among males as well as females. A positive correlation was seen as the fasting insulin levels and the HOMA-IR values were more in subjects with more severe acne.
Conclusion: Education about acne is necessary in schools and among the public, so that one knows where to seek appropriate advice and receive early effective treatment so as to prevent complications, both transient and permanent.

Keywords: Acne vulgaris, HOMA-IR, glycemia, BMI

Introduction
Acne vulgaris is a multifactorial disease affecting the pilosebaceous unit. It is characterized by a variety of skin lesions including comedones, papules, pustules, nodules, cysts and scars [1]. Acne is one of the most common skin disorders worldwide and occurs primarily at puberty with a prevalence of almost 95% in India [2]. Lesions clinically seen can be either non-inflammatory lesions (open and closed comedones) or inflammatory lesions (papules, pustules, and nodules). Complications include varying degrees of scarring and hyperpigmentation [3].
Several aggravating factors have been proposed in the pathogenesis of acne. It is seen that high glycemic load diets may exacerbate acne (also, Low Glycemic Load diet results in the improvement of acne lesions). High glycemic index food products are rapidly absorbed, increase serum glucose levels and stimulate increased glucose-dependent insulin signaling. Such hyperinsulinemia diets affect follicular epithelial growth and keratinization (hyperproliferation) and have an influence on androgen-mediated sebum secretion (due to androgen receptors in sebaceous glands), which is an essential and pivotal factor in the pathogenesis of acne vulgaris[4]. In other words, increased level of insulin in the plasma stimulates the secretion of androgens and causes an increased production of sebum, growth of the sebaceous glands and hyper-keratinization, which plays a fundamental role in pathogenesis of Acne Vulgaris (AV). High plasma levels of insulin-like growth factor 1 (IGF-1) which are caused by consumption of milk and dairy products, stimulates proliferation of sebocytes, resulting in the development and progression of acne lesions.

Skim milk contains less estrogen than whole milk. Estrogen is a hormone that may reduce acne [5].

This study was conducted to analyse the clinico-epidemiological profile of acne vulgaris and its relationship with insulin resistance among males and females.

Material and Method

The present cross sectional observational study was conducted in the department of Dermatology, Venereology and Leprosy at Chattrapati Shivaji Subharti Hospital from November 2018 to April 2020 for 1 and a half years after approval by the university. The study consisted of 500 clinically diagnosed patients of acne vulgaris attending the out-patient department. Patients were enrolled in the study after obtaining written informed consent and approval from Institutional Ethical Committee. Patient aged 11-40 years presenting with acne, all grades of acne including severe variants of acne and acne with acne scars were included in the study. Patients not willing to take part in the study and acne patients with known history of mental disorder unrelated to acne, concurrent physical illnesses and disabilities that can affect their mental state were excluded from the study.

General physical examination including BMI, anthropometry which includes height, weight, triceps skin thickness and waist/hip ratio was done. A detailed history was taken regarding the age, occupation, onset, course, site and duration of acne, history of associated symptoms, history of physical and mental stress, family history of acne, history of use of any drugs (oral or topical) especially steroid use, history of systemic diseases, diet, menstrual history and obstetric history, personal habits, and any other relevant skin or systemic disease.

Investigations comprised of fasting blood sugar and fasting insulin levels. These assess the insulin resistance based on HOMA-IR. HOMA-IR stands for Homeostatic Model Assessment of Insulin Resistance. In the study, the Optimal value is taken to be 1.0 (range=0.5–1.4). The HOMA-IR was calculated with the following formula:

HOMA−IR = Glucose X Insulin/22.5 (glucose levels in mmol/L, insulin levels in mIU/L)

HOMA-IR = Glucose X Insulin/405 (Fasting glucose in mg/dl, insulin in µIU/ml)

Data was collected in structured data collection forms. All the findings and observations were coded and entered in Excel master sheet.

Statistical analysis

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). For each assessment point, data were statistically analysed using factorial analysis of variance (ANOVA). Difference between two groups was determined using chi square test and the level of significance was set at $p<0.05$.

Results

Out of 500 subjects, 262 (52.4%) were males and 238 (47.6%) were females. The mean age of the study group was 21.63 years. Out of total 500 cases, maximum number of cases were found in the age group of 16-20 years (54%). 16–20 years was the most common acne affected age group among males (60.31%) as well as females (47.06%) while the least affected age group was 31-35 years in males (0.76%) and 36-40 years in females (4.62%).

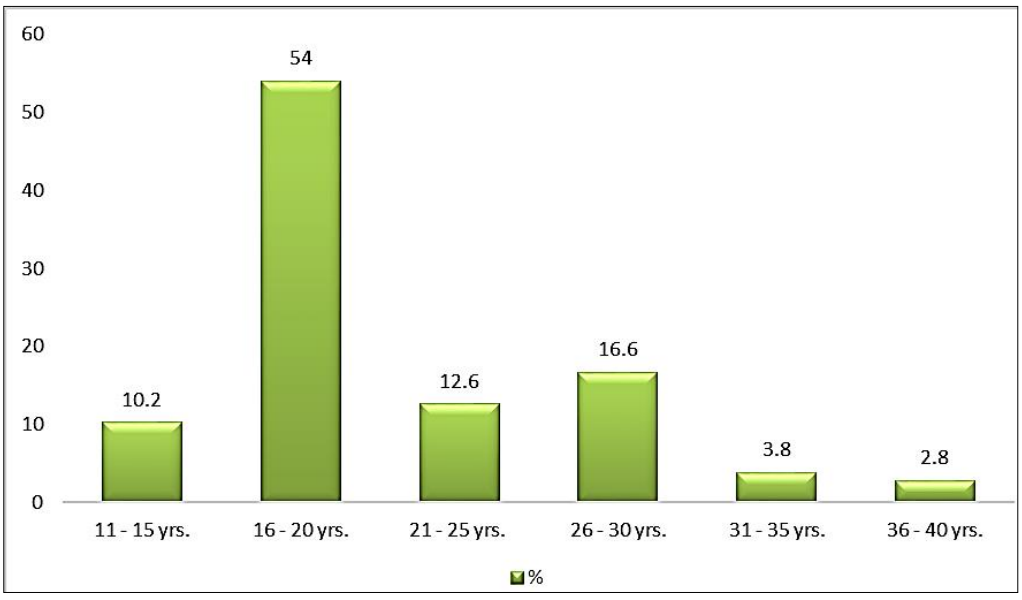

Fig 1: Distribution of acne vulgaris according to age in the study population

Normal BMI was more commonly seen in female patients with acne. 170 patients (34%) are found to be in the overweight category (BMI>25 kg/m^2). Out of these, majority are males (65.29%) being maximum in obese class I. Males with BMI>25 kg/m^2 reported more acne vulgaris as compared to females with statistically significant difference as $p<0.01$ by chi square test as shown in table 1.

Table 1: BMI status among the study subjects

BMI (Kg/m^2)	Male (N=262)		Female (N=238)		Total (N=500)	
	N	%	N	%	N	%
Underweight (<18.5)	25	9.54	32	13.45	57	11.4
Normal (18.5-24.9)	126	48.09	147	61.76	273	54.6
Pre-Obese (25-29.9)	77	29.39	51	21.43	128	25.6
Obese Class 1 (30-34.9)	20	7.63	4	1.68	24	4.8
Obese Class 2 (35-39.9)	9	3.44	3	1.26	12	2.4
Obese Class 3 (≥40)	5	1.91	1	0.42	6	1.2
p value	<0.01*					

*: Statistically significant

In the study, elevated lesions were reported by all the males and females (100%). Oily skin and erythema was reported more among females while pustules and nodules/Cyst were complained more among males (table 2).

Table 2: Presenting complaints among study subjects

Complaints	Male (N=262)		Female (N=238)		Total (N=500)	
	N	%	N	%	N	%
Oily Skin	217	82.82	213	89.50	430	86
Elevated Lesions	262	100.00	238	100.00	500	100
Pustules	211	80.53	163	68.49	374	74.8
Nodules/Cyst	161	61.45	71	29.83	232	46.4
Pain/Itching/Burning	69	26.34	63	26.47	132	26.4
Erythema	223	85.12	214	89.92	437	87.5

Out of the total, 54.4% of individuals complained of always suffering from stress due to any cause. This showed that stress is a major aggravating factor in causing acne as most of the patients suffered from stress at some point. Stress was not found among 16.03% and 12.18% of the males and females respectively with statistically significant difference (p value=0.04). Overall, males underwent more stress than females. 53.84% of the patients consuming High Glycemic diet were males and rest females. Cosmetics use was reported among 34.73% of the males and 71.43% of the females. The difference was statistically significant with *p*=0.008 by chi square test showing that cosmetics are more in common use by women having acne. 119 patients (23.8%) reported aggravation with seasonal variation. Out of these, majority (90.76%) complained of summer aggravation of acne. Only 11 patients reported aggravation in winters; 4 were males and 7 females. No statistically significant difference was seen among males and females. Premenstrual flare was revealed among 62.61% of the females. Medications were used by 13.6 % of total population with no statistically significant difference between males and females (table 3).

Table 3: Distribution of cases according to aggravating factors

Aggravating factors	Male (N=262)		Female (N=238)		Total (N=500)	
	N	%	N	%	N	%
Stress						
Always	133	50.76	139	58.40	272	54.4
Occasional	87	33.21	70	29.41	157	31.4
Absent	42	16.03	29	12.18	71	14.2
p value	0.04*					
Type of food						
Oily Food+ Intake of Meat + High Glycemic Diet	210	80.15	180	75.63	390	78
Vegetable and Fruit	52	19.85	58	24.37	110	22
p value	0.03*					
Cosmetics						
Yes	91	34.73	170	71.43	261	52.2
No	171	65.27	68	28.57	239	47.8
p value	0.008*					
Season						
Summer	57	21.76	51	21.43	108	21.6
Winter	4	1.53	7	2.94	11	2.2
Premenstrual Flare	-	-	149	62.61		
Medication	37	14.12	31	13.03	68	13.6
Deleterious habit						
None	171	65.27	224	94.12	395	79
Smoking	62	23.66	9	3.78	71	14.2
Alcohol	29	11.07	5	2.10	34	6.8
p value	0.03*					

*: Statistically significant

In our study, acne vulgaris was found on face among 80.25% of the females which is comparatively high as compared to males (58.02%). Back, chest and arms were more commonly involved in males as compared to females. Statistically significant difference was found among males and females with regard to location of lesions (*p*=0.02) as shown in table 4.

Table 4: Distribution of cases according to location of lesions

Location	Male (N=262)		Female (N=238)		Total (N=500)	
	N	%	N	%	N	%
Face	152	58.02	191	80.25	343	68.6
Face, Back, Chest	51	19.47	18	7.56	69	13.8
Face, Arm	12	4.58	8	3.36	20	4
Face, Back	30	11.45	14	5.88	44	8.8
Face, Chest	11	4.20	6	2.52	17	3.4
Back, Chest, Arm	6	2.29	1	0.42	7	1.4
p value	0.02*					

*: Statistically significant

In our study, it was seen that HOMA-IR value increased with the grade of acne, that is, insulin resistance showed a positive association with severity of acne. Mean HOMA-IR was found more in grade IV acne among males as well as females. The association between acne severity and insulin resistance was not found to be significant in either males or females (p=0.18 and 0.23, respectively, as calculated by ANOVA test). Inspite of this, a positive correlation was seen as the fasting insulin levels and the HOMA-IR values were more in subjects with more severe acne. No significant difference was found in between males and females in association with HOMA-IR (p<0.05 for each grade of acne, as calculated by unpaired t-test) (table 5).

Table 5: HOMA-IR comparison among the study subjects according to acne grading

Acne grading	Male (N=262)		Female (N=238)		*p* value
	Mean HOMA-IR	SD	Mean HOMA-IR	SD	
Grade I	1.6	2.09	1.5	1.35	0.39
Grade II	1.7	1.93	1.7	1.44	0.83
Grade III	2	1.86	1.9	1.81	0.64
Grade IV	2.2	1.92	2	1.40	0.12
Anova Test	1.91		1.29		
p value	0.18		0.23		

Discussion

It is essential to explore the disease burden of acne in hospitals with evaluation of the clinical profile and treatment pattern from time to time[1]. Such studies are necessary to evaluate the clinico-epidemiological profile, disease burden, and outcome with various modalities of treatment and also to reduce adverse consequences like scars and pigmentation. Hence, this study was aimed to find out and ascertain different clinical presentations of Acne vulgaris in both the sexes of various age groups.

In present study, out of 500 subjects, 52.4% and 47.6% were males and females respectively. Pooja Pandey *et al.* [6] in their study found that there was a male preponderance with ratio of 1.04:1 which is similar to our study. Waqar Al-Kubaisy *et al.* [7] reported that there was a significantly higher rate of acne among male students than that among females. Similar findings were seen in the study done by Smithard *et al.* [8] wherein out of the total number of 300 patients between age group 16 to 35 years, 153 patients (51%) were males and 147 patients (49%) were females. One of the reasons for male preponderance can be attributed to the fact that men increased sebum production.

In the present study, 16-20 years was the most affected age group from acne vulgaris among males (60.31%) as well as females (47.06%) while the least affected age group was 31-35 years in males (0.76%) and 36-40 years in females (4.62%). Similar results were observed in the study by Pandey P *et al.* [6]. Pandey P *et al.* [6] revealed that majority (71% of participants) belonged to age group of 18 to 25 years with majority of students and 11.3% patients belonged to age group 26 to 35 years.

The relation between acne formation and BMI has been studied by many authors. They found that acne was more prevalent among obese persons in women. In our study, 48.09% and 61.75% of the males and females respectively, have normal BMI. Males with BMI>25 kg/m^2 reported more acne vulgaris as compared to females with statistically significant difference as p<0.05. Waqar Al-Kubaisy *et al.* [7] detected that obese students of both sexes tends to have higher acne rate. This can be explained by the fact that obesity leads to increase in androgens and there is also psychological stress from being overweight which in turn causes surge of stress hormones that can worsen the acne.

In the present study, it was seen that high glycemic diet and oily food intake was taken by 78% of patients out of total 500. It was also comparatively more among males (80.15%) as compared to females with statistically significant difference. Acne is greatly influenced by the nutritional status of the patient. Essential fatty acids (linoleic acid and linolenic acid) deficiency causes follicular hyperkeratosis in the pilosebaceous duct, and increases the trans epidermal water loss in the skin of acne patients. This supports the suggestion that acne vulgaris might be aggravated by the consumption of a diet rich in saturated fats and monosaturated acids and low in poly unsaturated fatty acids. A high glycaemic diet induces hyperinsulinemia also results in androgen synthesis. Diet induced hyperinsulinemia also increases level of IGF-1 (Insulin-Like Growth Factor) and reduces IGF binding proteins. The increased free IGF-1 level results in unregulated growth of follicular epithelium, increased sebum production and synthesis of androgens from gonads [9].

In the present study, cosmetics use was reported among 34.73% of the males and 71.43% of the females. Similar results were revealed in other studies showing that increased use of cosmetics may play a role in increased prevalence of adult acne in women [10].

In our study acne problem was reported more in summer season as compared to winter, with no difference among males and females. Summer season and sun exposure act as aggravating factors in 28.4% and 23% of patients respectively in a study by Geeta Sharma *et al.* [10]. In an Indian study in 80.62% patients, summer aggravation of acne was seen. It is possible that UV radiation, which may cause inflammation and generate squalene peroxides which are highly comedogenic may play a role in the persistence of acne in tropical countries in addition to sweating and increased humidity. Like our study, Adityan B and Thappa

DM [11] found in their study that seasonal variation was observed only in 80 patients (25.9%); 71 patients (23%) exacerbated in summer and 9 (2.9%) in winter. This observation was against the conventional view that acne vulgaris exacerbates in winter and improves in summer.

Premenstrual flare was revealed among 62.61% of the females of the present study. In a study by Geeta Sharma *et al.* [10], premenstrual flare was noticed in 62.7% of the 225 female patients, which is in accordance with our study. In the study of Stoll *et al.* [12], 44% of 400 female participants reported premenstrual flares of their acne in the questionnaires. Although, there is a hypothesis about changes of surface lipid composition in the premenstrual phase, changes in hydration or the molecular structure of keratins or prostaglandin effects through its vasoactive properties. The exact hormonal cause for this flare is still not completely known and needs to be elucidated though further studies.

Acne as a part of syndromes like polycystic ovary Disease (PCOD) and hyper-androgenism, insulin resistance, acanthosis nigricans (HAIR-AN) indicate the positive correlation of insulin resistance and acne. The disease pathogenesis involves an interplay of various hormones including growth hormone (GH), insulin and insulin-like growth factor-1 (IGF-1) signaling during puberty. These lead to acne development by influencing adrenal and gonadal androgen metabolism. Hyperglycemic carbohydrates and insulinotrophic milk/dairy products have been identified to drive acne pathogenesis by promoting increased insulin/ insulin like growth factor-1 signaling. HOMA-IR is widely used as an index of insulin resistance. We had taken 2.5 as cut off value in the study. In our study, the mean HOMA-IR was found more in grade IV acne among males as well as females. It was seen that HOMA-IR value increased with the grade of acne, that is, insulin resistance showed a positive association with severity of acne. No significant difference was found in between males and females regarding HOMA-IR in our study. Prathima Munichandrappa reported similar results in their study [13]. They found no statistically significant difference between mean HOMA-IR of cases and controls in our study. This is similar to the results of studies by Balta *et al.* [14]. However a study by Nagpal *et al.* showed significantly high values of HOMA-IR in cases with acne compared to controls [15]. Since acne is a problem in adolescents, the early recognition of insulin resistance might help in better management of acne patients.

Our study has several limitations like its cross sectional design. In addition, the questions on stress were a subjective assessment. The relationship between the insulin resistance and Acne could not be elucidated and hence further studies with larger study population should be conducted for furtherance of the results obtained in this study.

Conclusion

This study brings out the clinical profile of acne vulgaris in a tertiary care hospital. The prevalence of acne, associations with other diseases, presence of aggravating factors and the grading/severity and distribution of lesions were studied in detail among the study population and the same compared between affected males and females. It is probable that not all teenagers who could benefit are accessing health care services for acne treatment. Further education about acne is necessary in schools and among the public, so that one knows where to seek appropriate advice and receive early effective treatment so as to prevent complications, both transient and permanent.

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