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Research Article

A Case Control Study of Insulin Resistance in Young Patients of Age Group 14-25 Years with Acne Vulgaris Attending Tertiary Care Center

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ABSTRACT

Background: The pathogenesis of acne vulgaris(AV) is multifactorial. Insulin resistance has been implicated in the pathogenesis of AV in few recent studies. Strong evidence of the association of insulin resistance with AV patients is lacking in the Indian population. This study was done to evaluate insulin resistance in young patients with AV. **Objectives**: To assess the prevalence of insulin resistance in patients aged 14-25 years with AV and to compare it between AV patients and controls. **Methodology**: The study group was recruited from patients attending the Dermatology department at a General Hospital for a period of 18 months to study the insulin resistance using the HOMA-IR index in the age group 14-25 years with and without AV. In this prospective case-control study, 50 cases of acne vulgaris with 50 healthy age and sex-matched controls were included. Patients were counselled and informed consent was taken. In each case, detailed history, local and systemic examination was done. Acne grading for each patient was done based on the Global Acne Grading System (GAGS). Samples for fasting blood sugar and fasting serum insulin levels were taken. HOMA-IR index > 2 was arbitrarily taken as insulin resistance. **Results**: Mean HOMA-IR Index in cases was 2.21 ±0.88 whereas in controls it was 1.50 ±0.58 ($p<0.05$). The prevalence of insulin resistance was significantly higher in cases (56%) compared with controls (12%) ($P = <0.001$). The prevalence of insulin resistance did not differ significantly among the acne severity groups. **Conclusions**: Insulin resistance has to be considered as a major determinant in the pathogenesis of AV. The insulin resistance may be a phase of prediabetes and may develop diabetes mellitus in the future. The patients of AV should be followed up to find out about the development of the metabolic syndrome. Further large scale studies are required in this aspect to evaluate insulin resistance in AV patients. Interventional studies are required regarding target therapies directed towards insulin resistance in the treatment of AV.

Key Words: *Acne vulgaris, Insulin resistance, HOMA-IR index, Prediabetes, Target therapy.*

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INTRODUCTION

Acne vulgaris (AV) is a common dermatologic disorder of the pilosebaceous unit predominantly affecting the adolescent age group and young adults. AV presents clinically as comedones, papules, pustules, nodules, and also may lead to sequelae like pigmentation and scars. It is mainly seen on the face, neck, trunk, and arms[1]. Definition of acne is widely variable[2]. In a study by Bloch, the presence of one comedone in a subject was considered as a case of acne[3]. According to Thiboutot Det al, acne was defined as the presence of a minimum of 15 comedones and a minimum of ten inflammatory papules[4].

AV affects more than 85% of the population at some stage of life with an earlier onset and more persistent nature in females[5]. Males have a higher incidence of more severe forms of acne[6].

The pathogenesis of acne is multifactorial[7]. The major pathogenic factors involved are excess sebum production, follicular hypercornification, propionibacterium acnes colonization of the follicle, and the release of local inflammatory mediators[8]. Additional factors in the pathogenesis of acne include genetic predisposition, hormonal abnormalities, immunological disorders, psychological, environmental, cosmetic, and iatrogenic factors[9,10]. High glycemic foods have been implicated in the pathogenesis of acne in recent studies and may be considered as one of the significant factors in the pathogenesis of acne[11,12,13]. There is a growing evidence in support of a high glycemic diet resulting in hyperinsulinemia and insulin-like growth factor-1 (IGF-1) signalling, which has got a significant role in the pathogenesis of acne during puberty[14].

In India, due to lifestyle changes, there is an increasing trend of metabolic syndrome, especially in adolescents and young adults. There are very limited studies to evaluate the role of glycemic factors and insulin resistance in patients with acne in the Indian population. Therefore, we conducted a case-control study evaluating the insulin resistance in young

patients of age group 14-25 years with acne vulgaris attending tertiary care centre.

MATERIALS AND METHODS

In this prospective case-control study, the study group was recruited from patients attending the outpatient and inpatient, Department of Dermatology at a General Hospital for a period of 18 months to study the insulin resistance using HOMA-IR index inthe age group 14-25 years with and without acne vulgaris. 50 cases of acne vulgaris with 50 healthy age and sex-matched controls were included in the study. Patients were counseled regarding the disease and informed consent was taken. A questionnaire form that contained information about their age, sex, weight, personal or familial history of acne, and eating habits was given to subjects before blood samples were collected. In each case, detailed history, thorough general physical, local and systemic examination was done. Acne grading for each patient was done based on the Global Acne Grading System (GAGS). Then blood samples were collected and sent to the laboratory to measure fasting blood sugar and fasting serum insulin levels. HOMA-IRindex was calculated based on the following formula:

$$\text{HOMA-IR} = \frac{\text{Fasting serum insulin in mU/l} \times \text{Fasting blood sugar in mg/dl}}{405}$$

HOMA-IR index > 2 was arbitrarily taken as insulin resistance in our study.

Inclusion criteria:

The subjects chosen were those attending Dermatology OPD. All consecutive newly diagnosed cases of acne vulgaris in the age group between 14-25years attending Department of Dermatology at a General Hospital who consented for the study in the age group between 14-25years were included in the study.

Exclusion criteria:

1. Diabetes mellitus/thyroid disorder.
2. Treatment with oral retinoids
3 Subjects with a history of smoking/ alcohol
4. Pregnancy

Results

In our study, 50 cases and 50 controls in the age group between 14-25 years were included.

Age group

Among the cases, the majority belonged to the age group of >21 years age group, n=22(44%) followed by 19-21 years age group, n=21(42%).

Gender distribution

Out of 50 cases, 26 (52%) were females and 24 (48%) were males.

Duration of acne

In our study, the majority of the cases had the diseases of 6-12 months duration, n=35(70%), followed by 13-18 months, n=8 (16%). We also had 5 cases i.e., 4% with onset of duration of less than 6 months.

Family history

Family history of acne was reported by 27 (54%) cases while it was reported by 22(44%) controls. ($p>0.05$)
Family history of diabetes mellitus (DM) was reported by 16 (32%) cases while it was reported by 25 (50%) controls in our study. ($p>0.05$)

BMI

Mean BMI in cases was 24.13 ±2.93 whereas in controls it was 23.47 ±2.45. When we compared the mean values of cases and controls, it was observed that there is no statistically significant difference in the mean values of both groups ($p>0.05$).

Grading of acne

Grade II acne was observed in 29 patients i.e. 58%. This is followed by grade I in13 (26%) patients. (Table 1)

Table 1: Distribution of Cases according to the grading of Acne (N=50)

Grading of Acne	Number	Percent
1	13	26.0
2	29	58.0
3	7	14.0
4	1	2.0

Fasting blood sugar (FBS), Fasting serum insulin (FSI), and HOMA-IR index

Comparison of FBS, FSI, and HOMA-IR Index between Study Groups (Table 2)

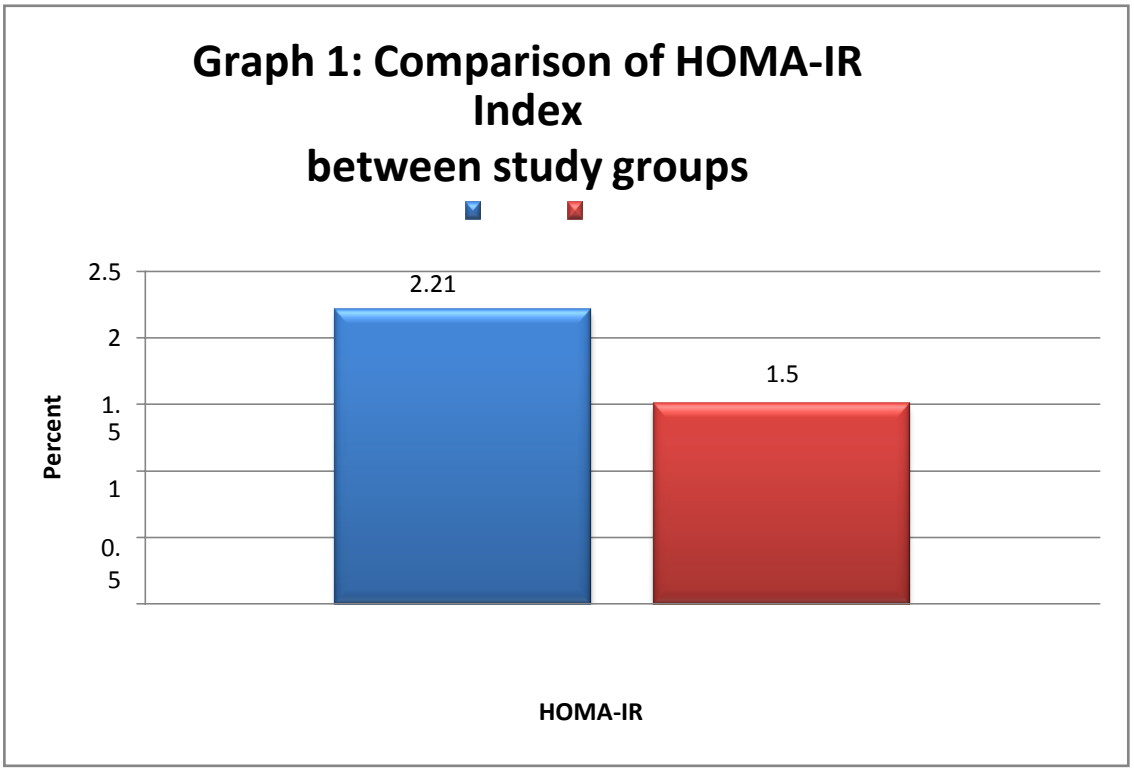
Mean fasting blood sugar in cases was 95.46±15.60 whereas in controls it was 85.46 ±8.17. When we compared the mean values of cases and controls, it was observed that there is a statistically significant difference in the mean values of bothgroups. ($p<0.05$)

Mean fasting serum insulin in cases was 9.44 ±3.86 whereas in controls it was 7.24 ±2.9. When we compared the mean values of cases and controls, it was observed that there is a statistically significant difference in the mean values of bothgroups. ($p<0.05$)

Mean HOMA-IR Index in cases was 2.21 ±0.88 whereas in controls it was 1.50 ±0.58. (Graph 1) When we compared the mean values of cases and controls, it was observed that there is a statistically significant difference in the mean values of bothgroups. ($p<0.05$)

Table 2: Comparison of FBS, FSI, and HOMA-IR Index between Study Groups(N=100)

Parameter	Group		P Value
	Cases (n=50) Mean (SD)	Controls (n=50) Mean (SD)	
FBS	95.46 (15.60)	85.46 (8.17)	<0.001*
FSI	9.44 (3.86)	7.24 (2.90)	0.002*
HOMA-IR Index	2.21 (0.88)	1.50 (0.58)	<0.001*
Unpaired t Test, P Value *Significant			



Comparison of FBS, FSI, and HOMA-IR Index between Grades of Acne

Table 3 shows there is no association between grading of acne and FBS, FSI, and HOMA-IR Index. (ANOVA, P Value Not Significant)

Table 3: Comparison of FBS, FSI and HOMA-IR Index between Grades of Acne (N=100)

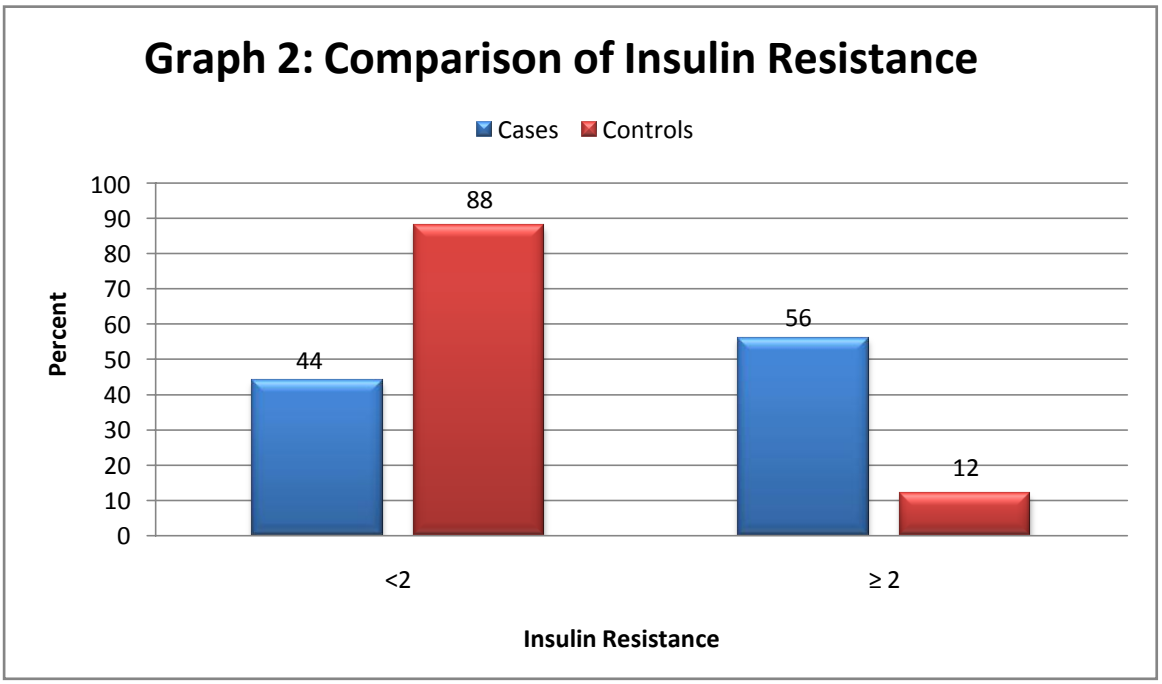
Parameter	**Grades of Acne Mean (SD)**				**P Value**
	1	**2**	**3**	**4**	
FBS	91.00 (16.35)	97.76 (16.81)	95.57 (7.13)	86.00	0.573
FSI	9.09 (4.85)	9.19 (3.64)	10.77 (3.07)	12.00	0.698
HOMA-IR Index	2.00 (0.98)	2.23 (0.89)	2.52 (0.64)	2.54	0.643
ANOVA, P Value Not Significant					

Insulin resistance

As previously mentioned, HOMA-IR > 2 was arbitrarily taken as insulin resistance. Prevalence of insulin resistance i.e, HOMA-IR index ≥ 2 was significantly higher in cases 28 (56%) compared with controls 6(12%) (P-value<0.001). (Table 4 and graph 2)

Table 4: Comparison of Insulin Resistance between Study Groups (N=100)

Insulin Resistance	**Group**	
	Cases (n=50) n (%)	**Controls (n=50) n (%)**
Not present	22 (44.0)	44 (88.0)
Present	28 (56.0)	6 (12.0)
Chi-Square Test, P Value <0.001, Significant		



CLINICAL PICTURES

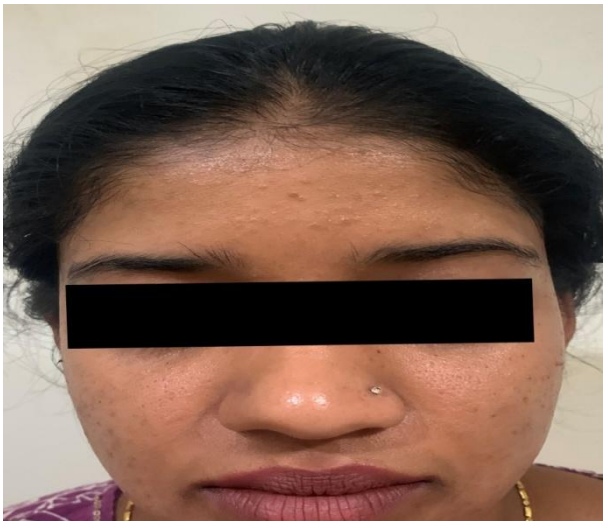


Figure 1 : Acne vulgaris grade I

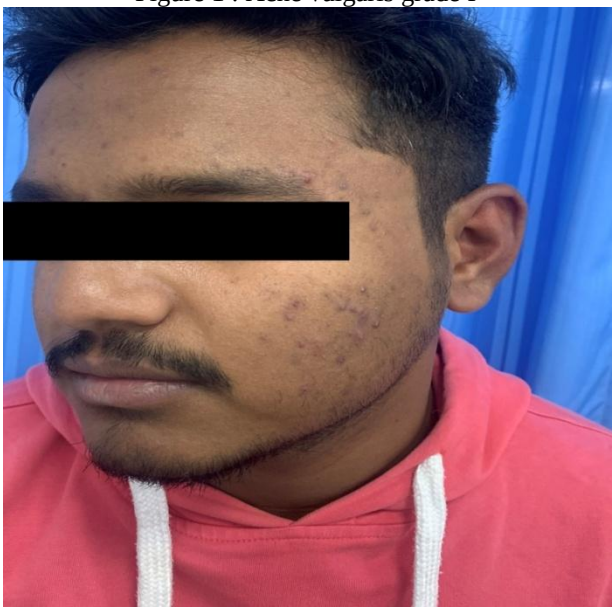


Figure 2 : Acne vulgaris grade II

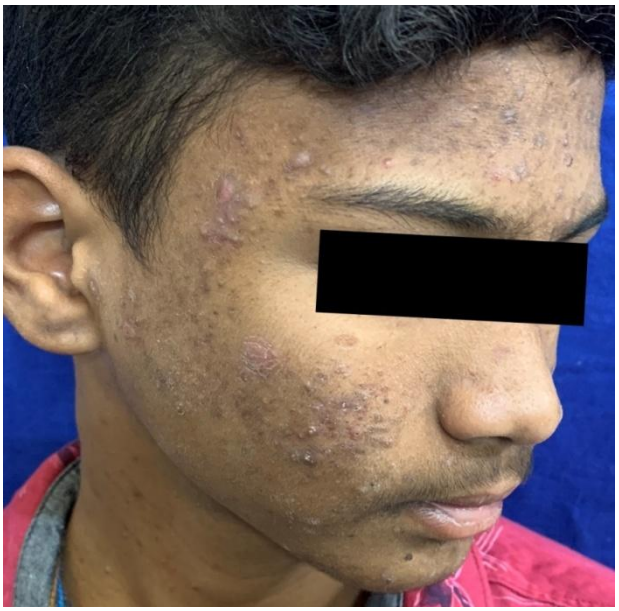


Figure 3 : Acne vulgaris grade III

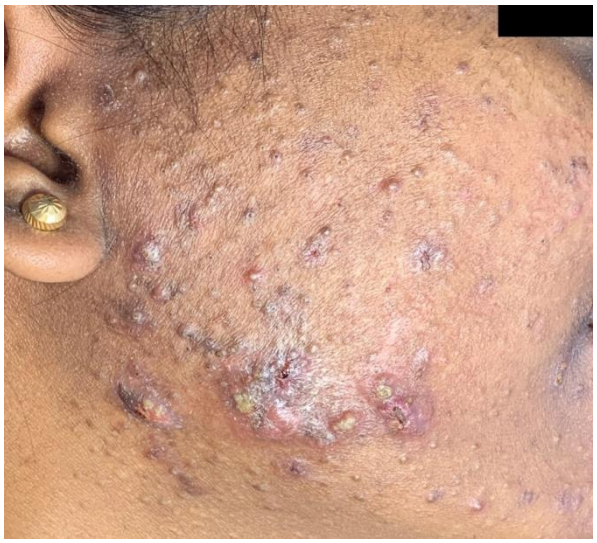


Figure 4: Acne vulgaris grade IV

DISCUSSION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous units[15]. It is believed to be the most common disease of the skin[16,17]. The condition usually starts in adolescence, peaks at the ages of 14 to 19 years and frequently resolves by mid- twenties. A total of 50 patients with acne vulgaris in the age group between 14-25 years were included in the study. The control group included 50 age-matched patients without acne but with other dermatological abnormalities attending the dermatology outpatient department.

Relationship between fasting plasma glucose and acne:

Mean fasting blood sugar in cases was 95.46±15.60 whereas in controls it was 85.46 ±8.17. When we compared the mean values of cases and controls, it was observed that there was a statistically significant difference in the mean values of both groups. ($p<0.05$).

In similarity to our study, a study by Michela Del Prete et al[18] from Italy which included 22 patients with severe acne vulgaris and 22 healthy controls and found a significant difference in fasting blood glucose levels different between both the groups ($p<0.05$). The authors attribute this finding to the physiological insulin resistance state during puberty.

Mohit Nagpal et al[19] found that mean (SD) fasting plasma glucose levels were significantly higher in patients (88.2 ±8.3 mg/dL) than in controls (84.5 ±11.2 mg/dL)(P = .008). The mean fasting plasma glucose level in all individual

acne severity groups was higher than the mean fasting plasma glucose level in controls. The authors correlated this variation among different acne severity to the prevalence of metabolic syndrome in various severities. This study was also similar to our study.

In contrast to our study, Nazan Emiroglu et al[1] in their case-control study including 243 acne patients and controls did not find any statistically significant difference between the case and control group. ($p > 0.05$, 82.91 ±9.76 in cases vs. 80.26 ±8.33in controls). The authors observed significant insulin resistance in patients with acne indicating non-dietary source of hyperinsulinemia in the pathogenesis of acne.

Our study showed a significant difference in fasting serum glucose levels in acne patients. This may be attributed to the high glycemic diet intake of the patients, which should be considered as an environmental risk factor in the pathogenesis of acne.

Fasting serum insulin level in acne vulgaris and comparison between cases and controls:

In our study, mean fasting serum insulin in cases was 9.44 ±3.86 whereas in controls it was 7.24 ±2.9. When we compared the mean values of cases and controls, it was observed that there was a statistically significant difference in the mean values of both groups.($p<0.05$)

Similar to our study, Michela Del Prete et al[18] reported that 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). Recruiting treatment-resistant acne patients in this study could have led to the variation from our study.

Arvind Verma et al[20] reported that out of 300 patients, 86 acne patients had elevated levels of serum insulin (28.7%) while remaining 214 (71.3%) demonstrated normal levels. The authors attribute this observation to high glycemic diet prevalent among acne patients in their study group.

Munichandrappa P et al[21] have reported fasting insulin levels of 8.0 ± 3.2 in cases and 6.8 ± 3.3 in controls. There was no significant difference in the mean fasting insulin level of cases and controls (p-0.05). This was contrasting with the findings observed in our study.

Mohit Nagpal et al[19] found that mean (SD) fasting insulin levels in cases (9.2±8.5 mg/dL) and controls (7.8 ±6.8 mg/dL) were statistically insignificant. Prevalence of metabolic syndrome ($P = .38$) did not differ among the acne severity groups. This was in contrast to our study.

Kaymak et al[22] studied a group of 49 patients with acne and 42 healthy control subjects and concluded that there are no significant differences in the levels of serum fasting glucose, insulin, and leptin. They also reported that no significant differences could be identified among all acne groups according to fasting glucose and insulin levels which were dissimilar to our study.

Our study has found a statistically significant difference in fasting insulin levels between cases and controls. This suggests that along with environmental and hormonal factors, hyperinsulinemia should be considered in the pathogenesis ofacne.

HOMA-IR index in acne vulgaris and comparison between cases and controls: Homeostasis model assessment of insulin resistance (HOMA-IR) is one of the indicators used to assess the insulin resistance. It is calculated by the following formula

$$\text{HOMA-IR} = \frac{\text{Fasting serum insulin in mU/l} \times \text{Fasting blood sugar in mg/dl}}{405}$$

HOMA-IR index > 2 was arbitrarily taken as insulin resistance in our study.

Mean HOMA-IR Index in cases was 2.21 ±0.88 whereas in controls it was 1.50 ±0.58. When we compared the mean values of cases and controls, it was observed that there was a statistically significant difference in the mean values of both groups. ($p<0.05$**)**. The mean (SD) HOMA-IR value in cases was significantly higher (2.21 [0.8]) than in controls (1.5 [0.58]).

INSULIN RESISTANCE

A HOMA-IR value greater than 2 was arbitrarily considered as insulin resistance in our study. Prevalence of insulin resistance was significantly higher in cases 28 (56%) compared with controls 6(12%) (P-value <0.001). This indicates the prevalence of insulin resistance was higher in cases as compared to controls.

A study by Mohit Nagpal et al[9] showed that mean(SD) HOMA-IR index was 2.0 (1.8) among cases and 1.7 (2.3) among controls (p<.04). A study by Del Prete et al[18] showed that mean(SD) HOMA-IR index was 1.7 (0.8) among cases and 1.1 (0.3) among controls. (p=.01). A study by Balta et al[23] showed that mean (SD) HOMA-IR index was 2.0(1.2) among cases and 2.1(0.8) among controls. (p=0.51).

HOMA-IR depends on the product of fasting plasma glucose and insulin levels. The mean HOMA-IR value was significantly higher in cases. However, the HOMA-IR value was comparable among acne severity groups. Significantly higher prevalence of insulin resistance, which was predefined as a HOMA-IR value greater than 2, was observed in cases. However, insulin resistance in more severe acne compared with mild acne was not different significantly. The previous studies on HOMA-IR in acne are summarized in table 5.

Table 5: Findings of the previous studies by Mohit Nagpal *et al*[19], Del Prete *et al* [18] and Balta *et al*[23]

Study by Mohit Nagpal *et al*[19] Mean(SD) HOMA-IR index			Study by Del Prete *et al*[18], Mean (SD) HOMA-IR index			Study by Balta *et al*[23] , Mean (SD) HOMA-IR index		
Cases	Controls	*P* Value	Cases	Controls	*P* Value	Cases	Controls	*P value*
100	100		22	22		35	35	
22.7 (3.0)	23.7 (3.0)	.06	18.6 (2.5)	20.2 (3)	.06	30.8 (5.4)	30.8 (5.8)	.98
22.9 (4.0)	23.4 (3.2)	.37	24 (2.8)	20.1 (1.5)	.003	24.6 (4.0)	25.0 (4.1)	.68
85.3 (9.4)	83.6 (7.4)	.17	86.8 (9.8)	83.4 (8)	.002	- - -	- - -	- - -
120.2 (10.3)	116.9 (9.1)	.01[a]	128.1 (7.9)	112.5 (9)	.0001	- - -	- - -	- - -
79.1 (7.0)	76.2 (5.9)	.002[a]	80.9 (6.4)	72.9 (7.8)	.001	- - -	- - -	- - -
88.2 (8.3)	84.5 (11.2)	.008[a]	88.9 (7.8)	84.3 (5.9)	.03	89.7 (7.4)	90.0 (12.6)	.90
42.5 (11.3)	40.8 (8.6)	.24	46.5 (8)	57.3 (8)	.001	53.4 (19.6)	53.0 (12.2)	.91
106.0 (54.2)	120.8 (53.6)	.05	83 (3.2)	78.5 (22.3)	.40	123.7 (94.6)	94.0 (59.5)	.12
9.2 (8.5)	7.8 (6.8)	.22	10.6 (8.4)	5.5 (1.4)	.01	9.0 (4.9)	9.8 (3.5)	.41
2.0 (1.8)	1.7 (2.3)	.04[a]	1.7 (0.8)	1.1 (0.3)	.01	2.0(1.2)	2.1(0.8)	.51
17	9	.09	36	0	- - -	- - -	- - -	- - -

CONCLUSIONS

In this study, the association of fasting blood sugar, fasting serum insulin and HOMA-IR index between cases and controls was statistically significant. Thus patients with acne were observed to be more prone to have a higher prevalence of insulin resistance compared with controls. However, the association of BMI levels between cases and controls was not significant. These observations suggest that insulin resistance has to be considered as a major determinant in the pathogenesisof acne vulgaris. The insulin resistance may be a phase of prediabetes and may develop diabetes mellitus in

the future. The patients of acne vulgaris should be followed up for a long time to find out about the development of conditions associated with insulin resistance. Further large scale studies are required in this aspect to evaluate the insulin resistance in acne vulgaris patients. Interventional studies are required regarding target therapies directed towards insulin resistance in the treatment of acne vulgaris.

Table 3: Comparison of FBS, FSI and HOMA-IR Index between Grades of Acne (N=100)

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	1	**2**	**3**	**4**	
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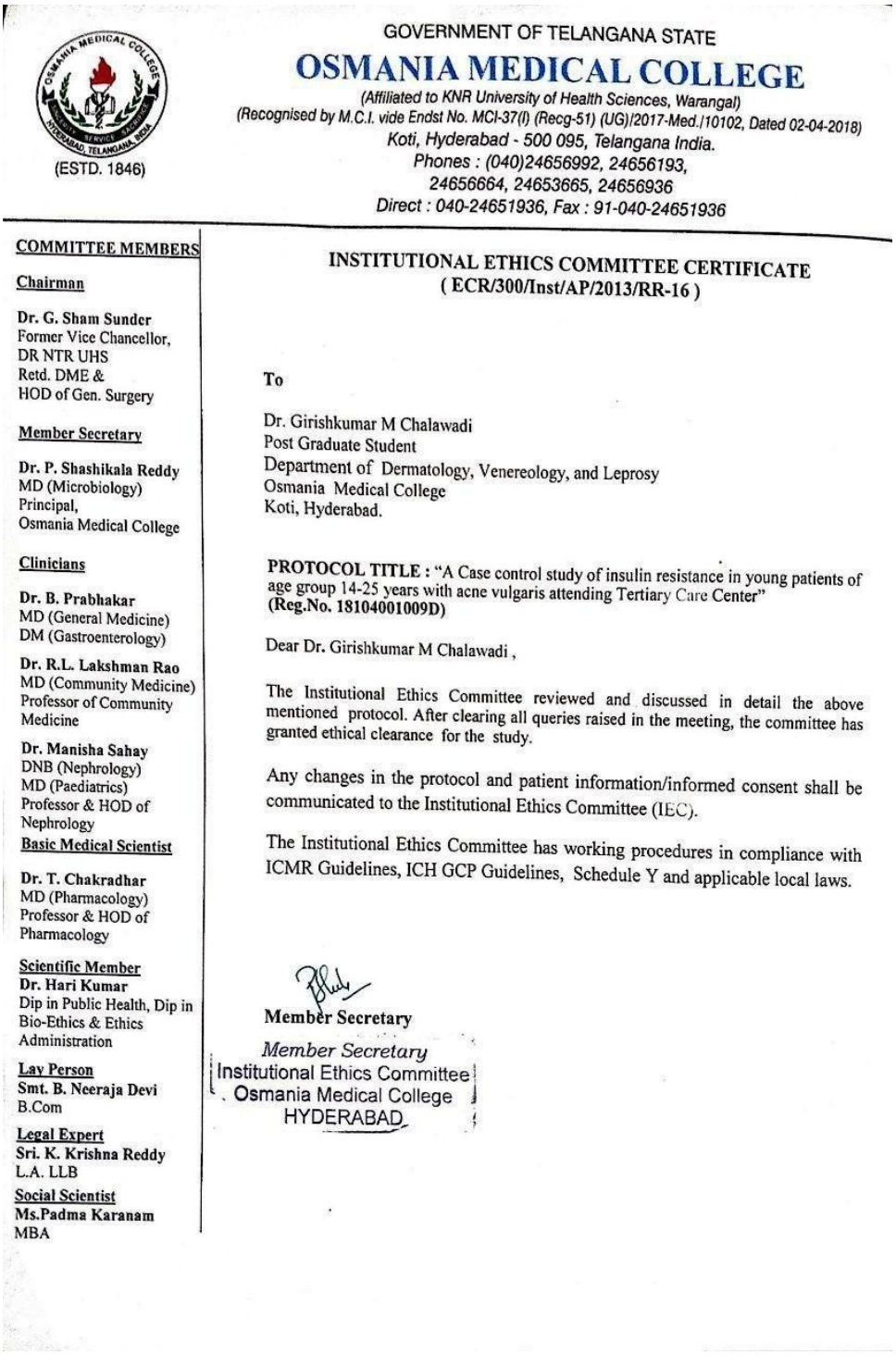
HOMA-IR Index	2.00 (0.98)	2.23 (0.89)	2.52 (0.64)	2.54	0.643
ANOVA, P Value Not Significant					

Ethics approval and consent to participate

- Ethics approval and consent was obtained.
- Include the name of the ethics committee that approved the study and the committee's reference number if appropriate
  Studies involving animals must include a statement on ethics approval.
  If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section – Not applicable



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To

Dr. Girishkumar M Chalawadi
Post Graduate Student
Department of Dermatology, Venereology, and Leprosy
Osmania Medical College
Koti, Hyderabad.

PROTOCOL TITLE : "A Case control study of insulin resistance in young patients of age group 14-25 years with acne vulgaris attending Tertiary Care Center"
(Reg.No. 18104001009D)

Dear Dr. Girishkumar M Chalawadi ,

The Institutional Ethics Committee reviewed and discussed in detail the above mentioned protocol. After clearing all queries raised in the meeting, the committee has granted ethical clearance for the study.

Any changes in the protocol and patient information/informed consent shall be communicated to the Institutional Ethics Committee (IEC).

The Institutional Ethics Committee has working procedures in compliance with ICMR Guidelines, ICH GCP Guidelines, Schedule Y and applicable local laws.

Member Secretary

Member Secretary
Institutional Ethics Committee
Osmania Medical College
HYDERABAD

List of abbreviations
AV- Acne vulgaris
HOMA-IR INDEX- Homeostatic Model Assessment of Insulin Resistance
IGF-1-Insulin like growth factor-1
FBS- Fasting blood sugar
FSI- Fasting serum insulin

Conflicts of Interest: "The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper."

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Authors' contributions: The individual contributions of authors to the manuscript should be specified in this section.

"Chalawadi analyzed and interpreted the patient data regarding the demographic data, associated diseases and the HOMA-IR index. J performed the clinical examination of the patients, along with blood sample collection and was a major contributor in writing the manuscript. All authors read and approved the final manuscript."

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