

## Insulin resistance in adult acne: A cross-sectional study from a tertiary care centre in south India

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### ABSTRACT

**Background:** Adult acne is acne beyond 25 years of age. Recent studies point to the positive correlation between adult acne and insulin resistance. Aims and objectives of this study was to evaluate insulin resistance using homeostasis model assessment of insulin resistance (HOMA-IR) index in adult acne and also to correlate insulin resistance with respect to severity of adult acne.

**Methods:** This cross-sectional study included 80 patients with adult acne. The severity of acne was assessed by global acne grading score (GAGS). Serum fasting blood sugar levels and fasting insulin levels were measured in these patients. HOMA-IR index was calculated. Descriptive statistics like frequency, percentage, mean and standard deviation were used for statistical analysis. Correlation between insulin resistance and severity of acne was measured by Spearman rank correlation coefficient.

**Results:** Eighty patients were enrolled in the study. Of this, 82.5 % (n=66) had mild acne, 13.8% (n=11) patients had moderate acne and 3.8% (n=3) had severe acne. Among this 43 (53.8%) patients had cutaneous features of hyperandrogenism. A significantly higher proportion of females had mild acne compared to males. Mean fasting blood sugar level, fasting insulin level and HOMA-IR index were 85.73 +/- 8.055mg/dl, 7.69 +/- 2.68  $\mu$  IU/ml and 1.62 +/- 0.58 respectively. There were no correlation between those parameters and severity of adult acne. Only 3.8% patients had insulin resistance (n=3).

**Conclusion:** In our study only 3.8% (n=3) had insulin resistance. There was no correlation between insulin resistance and severity of adult acne. So according to our study, insulin resistance have no significant role in adult acne.

**KEYWORDS:** adult acne, HOMA-IR, insulin resistance, metabolic syndrome

### INTRODUCTION

Adult acne also known as post-adolescent acne is acne that affects adults older than 25 years. Acne persisting beyond the age of 25 years is called persistent acne and developing for the first time after the age of 25 years is called late onset acne.<sup>1</sup> Recent studies point to the positive correlation between adult acne and insulin resistance.<sup>1</sup> Insulin resistance is a predictor of cardiovascular diseases, hypertension, diabetes, obesity, and

metabolic syndrome. The prevalence of both metabolic syndrome and acne have increased in recent past.<sup>2</sup> Early detection and intervention of this condition can prevent metabolic complications and associated mortality. This research was done to examine the clinical profile of patients who presented with adult acne and also to examine the correlation between the severity of adult acne and insulin resistance.

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## METHODOLOGY

This hospital based cross-sectional study was conducted in out patient department of dermatology in a tertiary care center in south India. Study included 80 patients with acne vulgaris older than 25 years. Aims and objectives of the study were to evaluate insulin resistance using Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index in adult acne and to correlate insulin resistance with respect to severity of adult acne.

After obtaining written informed consent, detailed history was taken, clinical examination done and photographs were taken. The severity of acne was assessed by global acne grading score (GAGS). Serum fasting blood sugar levels and fasting insulin levels were measured in these patients. Serum insulin level was measured by using electrochemoluminescence method (Siemens, Germany), with a reference range of 2.6-24.9  $\mu\text{U}/\text{mL}$ . HOMA-IR index was calculated according to the formula: fasting glucose (mg/dL) X fasting insulin (mU/L) / 405. HOMA-IR value  $>2.5$  taken as Insulin resistance. Descriptive statistics like frequency, percentage, mean and standard deviation were used for statistical analysis. Correlation between insulin resistance and severity of acne was measured by Spearman rank correlation coefficient. All p values  $<0.05$  were considered significant.

## RESULTS

A total of 80 adult patients with acne were included in the study. Out of 80, 15 (18.8%) were males and 65 (81.3%) were females. Mean duration of acne was  $9.01 \pm 6.842$  years. Mean age of patients were  $30.95 \pm 5.717$  years. 58 (72.5%) patients had persistent acne while 22 (27.5%) had

late onset acne. Mean onset of adult acne was at age of  $21.33 \pm 6.7$  years. Using Chi-square test, there was no significant association between severity and persistence acne as well as late onset acne.

Most common manifestation was papule (98.8%) followed by comedones (67.5%). Pustules were seen in 27(33.8%) patients. Nodules were present in 13 (16.3%) patients. Inflammatory lesions and non-inflammatory lesions were seen in 98.75% and 67.5% of patients respectively.

Out of the total 65 females in the study, 21 (26.3%) patients had irregular cycles. In this 40 (50%) patients reported premenstrual flare of acne. Five patients (6.3%) patients had history of treatment taken for infertility and 12 (15%) had polycystic ovarian syndrome (PCOS) of which 7 (8.8%) were on oral contraceptive pills (OCP). More than 25% of patients had family history of adult acne, while nearly 50% of patients had family history of diabetes.

Only 2.5% of the adult acne patients had obesity. There was no significant association between BMI and severity of acne. ( $p=0.152$ ). There was a statistically non-significant weak positive correlation between BMI and global acne grading score (Spearman's correlation coefficient= $0.166, p=0.141$ )(Table 1).

**Table 1** Distribution of sample according to BMI

| BMI categories | kg/m <sup>2</sup> | Frequency | %    |
|----------------|-------------------|-----------|------|
| Underweight    | $<18.5$           | 4         | 5    |
| Normal         | 18.5–22.9         | 52        | 65   |
| Overweight     | 23.0–24.9         | 22        | 27.5 |
| Obese          | $\geq 25$         | 2         | 2.5  |

Using Kruskal-Wallis Test, there was a significant difference between mean BMI in these 3 group (p=0.016). Mean BMI of severe group is significantly higher than mild group (p=0.016). Majority of the patients, 82.5% had mild acne, 11(13.8%) patients had moderate acne and 3(3.8%) had severe acne. None of the patients had very severe acne (Table 2). Of this 43(53.8%) patients had features of hyperandrogenism in the form of seborrhea, acanthosis nigricans, androgenetic alopecia and hirsutism in 51.3% (n=41), 10% (n=8), 7.5%(n=6) and 6.3%(n=5) patients respectively (Fig 1). FBS of all patients were below 110 mg/dl. Mean fasting insulin level was 7.69±2.68 µIU/ml. Mean HOMA-IR index was 1.62±0.58 µIU/ ml (Table 3).

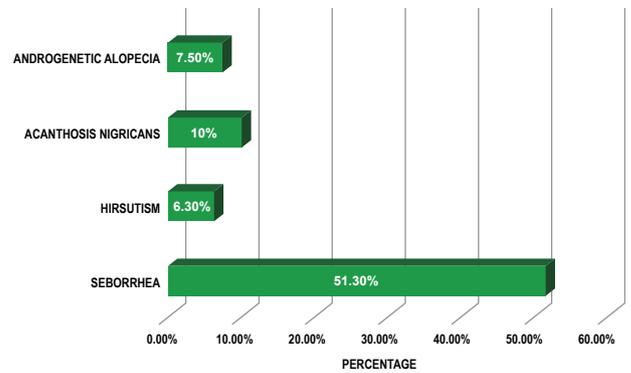


Fig. 1 Distribution of cutaneous manifestations of hyperandrogenism

**Table 2** Mean BMI according to severity of acne

| BMI      | Frequency | Mean         |
|----------|-----------|--------------|
| Mild     | 66        | 23.05+/-3.39 |
| Moderate | 11        | 24.35+/-2.93 |
| Severe   | 3         | 27.33+/-0.92 |

**Table 3** Descriptive statistics of the sample according to the HOMA-IR index

|                     |       |
|---------------------|-------|
| Mean                | 1.62  |
| Std. Deviation      | 0.58  |
| Median              | 1.535 |
| Interquartile Range | 0.7   |
| Minimum             | 0.6   |
| Maximum             | 4.6   |

Only 3.8% patients had insulin resistance (n=3). Out of three, 2 had mild acne and 1 had moderate acne. The Spearman’s correlation coefficient between IR and severity of acne was not significant.

Using Mann Whitney U test, there was no significant difference between the median HOMA IR scores of the 2 groups. The Spearman’s correlation coefficient between HOMA IR and severity of acne, between FBS and severity of acne, between fasting insulin level and severity of acne and between FBS and global acne score were not significant.

## DISCUSSION

Although acne usually declines after the age of 40 years, in our study, it was still present in 10% of patients. There were no cases of adult acne reported beyond the age of 45 in our study. This was similar to study by Rajegowda et al,<sup>3</sup> Khunger and Kumar.<sup>1</sup> Adult acne is more common in women. In our study women were predominantly affected (81.3%) as compared to men (18.8%). This might be because women are more concerned about these sort of lesions in their face and will seek medical attention than men.

Adult acne can either be persistent acne or late-onset adult acne. In our study, persistence of was seen in majority of patients (72.5%) than late-onset acne (27.5%). This was in concordance with study by Khunger and Kumar,<sup>1</sup> Goulden *et al*,<sup>4</sup> Swathi and Kusagur,<sup>5</sup> Rajegowda *et al*<sup>3</sup> and

Abrol and Sharma<sup>6</sup> who reported 82%, 73.2%, 70%, 77.3% and 82.7% of persistent acne respectively in their studies.

It is proposed that genetic factor plays an important role in adult acne. In our study more than 25% of patients had family history of adult acne, while nearly 50% of patients had family history of diabetes. Though all patients with severe acne in our study had family history of adult acne, association between family history and severity of acne was not statistically significant.

Hyperandrogenism is a known cause of acne. Patients with hyperandrogenism may have cutaneous features like seborrhea, hirsutism, androgenetic alopecia and acanthosis nigricans. These features are also seen in patients with PCOS. In our study, 53.8% patients had features of hyperandrogenism. Majority (51.3%) patients had seborrhea followed by acanthosis nigricans, 7.5% had androgenetic alopecia and 6.3% had hirsutism irrespective of PCOS. In these patients androgen stimulates sebaceous gland and resulted in acne. In a study by Rajegowda *et al*, 6.6% of patients had cutaneous features hyperandrogenism. Most common one was seborrhea, which was seen in 70.6% of patients. Then hirsutism in 30.6%, acanthosis nigricans in 21.3%, and androgenetic alopecia in 16%.<sup>3</sup> While Goulden *et al* reported 37% of women exhibiting cutaneous features of hyperandrogenism like hirsutism (24.2%) and androgenetic alopecia (7.2%).<sup>4</sup> Both these studies were comparable to our finding suggesting the role of hyperandrogenism in adult acne.

Out of the 65 females, 21 (26.3%) patients had irregular menstrual cycles and 50% of patients had premenstrual flare of acne. This is due to hormonal changes during this premenstrual pe-

riod, mainly androgen. Irregular menstrual cycle can be a part of PCOS. This was in accordance with the study conducted by Swathi and Kusagur,<sup>5</sup> Rajegowda *et al*,<sup>3</sup> Stoll *et al*<sup>7</sup> and Goulden *et al*<sup>4</sup> where premenstrual flare was observed in 46%, 74.7%, 44%, and 37% of patients, respectively. This was in contradiction to Khunger and Kumar who observed premenstrual flare in only 11.7% of patients.<sup>1</sup> In this study 5 females out of 80 had history of treatment taken for infertility, 12 patients (15%) had PCOS and 7 out of them were on OCP. PCOS is a condition that relates to acne and IR along with obesity, and hyperandrogenism. Acne is a common finding in PCOS patients. Out of 21 patients with irregular menstrual cycle only 12 patients had PCOS. This was different from Rajegowda *et al* were 58 patients (38.7%) had features of the polycystic ovarian disease (PCOD).<sup>3</sup> In a study by Khunger and Kumar were only 2 out of 230 had PCOs.<sup>1</sup>

The relationship between body mass index (BMI) and acne is still a controversy. BMI, acne and IR are linked to each other in PCOS and also by their common mTORC1 activation. Mean BMI of our study population was in normal ranges. But there was a significant difference in BMI in mild and severe acne patients. Patients with severe acne were obese. But we couldn't make a conclusion between their relationships as only 3 patients had severe acne.

We used the Global Acne Grading System (GAGS) to grade the severity of acne. This system divides the face and trunk into six areas (the forehead, right and left cheek, nose, chin, and the chest and back) and given a factor to each area and grades acne into mild, moderate, severe and very severe. Same was used by Munichandrappa *et al* in their study.<sup>8</sup> In our study majority of the

patients (82.5 %) had mild acne, 13.8% patients had moderate acne and 3.8% had severe acne. Whereas Munichandrappa et al reported 64.4% had moderate, 24.4% had mild and 11.1% had severe acne. In present study and study by Munichandrappa et al, none had severe acne.<sup>8</sup>

Studies have shown elevated blood glucose levels in acne patients. This is because hyperglycemia lead to hyperinsulinemia which decreases IGFBP-3, increases IGF-1 (insulin like growth factor) and their action on cell proliferation. High blood insulin level may exacerbate acne by increasing the basal keratinocytes proliferation. Hyperinsulinemia causes increased synthesis of androgens, leading to high sebum production. In our study, Mean FBS was 85.73 +/- 8.0 mg/dL. FBS of all patients were below 110 mg/dl. This may be because mean age of our population was 30.9. Mean insulin level was 7.69 +/- 2.6µIU/ml. We used HOMA-IR value for assessing IR. HOMA-IR index is widely used in assessing IR in clinical research. This test is based on fasting glucose and fasting insulin levels. Value > 2.5 suggests insulin resistance. Mean HOMA-IR index in our study was 1.62 +/- 0.58. It is believed that physiological IR developed during adolescents continued in adult acne. But in our study, only 3.8% patients had insulin resistance (n=3) with HOMA-IR index>2.5. Out of three, 2 had mild acne and 1 had moderate acne. This maybe because of small sample size. This was similar to Nagpalet al<sup>9</sup> and Del Prete et al<sup>10</sup> where mean FBS was 88.2 and 88.9, mean fasting insulin level was 9.2 and 10.6 and mean HOMA- IR 2.0 and 1.7 respectively.

Acne may also be a common component of many systemic diseases or syndromes which are also usually linked to IR especially when it comes to

adult acne. This is the case in SAHA (seborrhea, acne, hirsutism, alopecia), PCOS and HAIR-AN (hyperandrogenism, insulin resistance, acanthosis nigricans) syndrome. This all happens via IGF-1. Balta et al didn't find any significant differences between cases and controls of post-adolescent acne in fasting blood glucose, fasting insulin and the HOMA-IR index and there was no significant correlations between acne severity and fasting blood glucose (p=0.39), fasting insulin (p =0.07) or the HOMA-IR index (p=0.07)<sup>11</sup> Munichandrappa et al also couldn't elicit any statistically significant difference in mean fasting insulin levels among cases and controls. The difference among the mean HOMA-IR values was not statistically significant. There was no significant correlation between acne severity and fasting glucose and HOMA-IR values. But there was a weak positive correlation between acne severity and fasting insulin levels.<sup>8</sup>

According to Kaymak et al. serum glucose, insulin levels, and HOMA-IR indices in younger patients with acne vulgaris and control subjects did not differ significantly. Also as per them there is no any statistically significant association between acne severity and insulin resistance which is similar to the present study.<sup>12</sup>

Nagpal et al studied 100 male patients and controls with age 20-32 years. Mean FBS levels were significantly higher in patients than in controls (p = .008). However, mean fasting insulin levels were comparable between the cases and controls and statistically significant difference in prevalence of insulin resistance (p = 0.036) was there. But prevalence of insulin resistance (p= 0.55) did not differ among the acne severity groups.<sup>9</sup>

In study Conducted by Del Prete et al, 22 young

males with acne and equal number of controls were included. As compared to controls, higher BMI ( $p = 0.003$ ), serum insulin concentrations ( $p=0.002$ ), basal glucose concentrations ( $p=0.03$ ) and HOMA-IR ( $p = 0.016$ ) were observed in acne patients. In 13 patients with acne and BMI  $<24.9$  there was significant correlation between acne severity and HOMA-IR.<sup>10</sup>

Since adult acne cases are increasing day by day, we calculated insulin resistance with HOMA-IR in order to illuminate the role of insulin resistance in adult acne. We found that adult acne is not associated with insulin resistance. Also there were no significant differences between fasting blood glucose or fasting insulin levels, or HOMA-IR indices with respect to acne severity.

Our study population was limited in size owing to the restrictions caused by COVID pandemic. Also the number of patients with severe acne was very low compared to mild and moderate. So more studies with larger sample size are needed to prove correlation between adult acne and insulin resistance.

## CONCLUSION

Acne vulgaris is believed to be a multifactorial disease. A significantly higher proportion of females had mild severity compared to males, suggesting that there is an early consultation among women, as they are more concerned about cosmetic appearance. Though serum insulin levels were normal in our study, the abnormality could be in evolution which needs to be kept in mind. Even though there was no correlation between insulin resistance and severity of adult acne in our study, more studies with larger sample size are needed to prove the role of insulin resistance in adult acne. Acne should be obviously consid-

ered as a systemic disease, requiring a complex and individualized therapy.

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