



## Research article

## Analysis of correlation between insulin resistance and severity of acne vulgaris

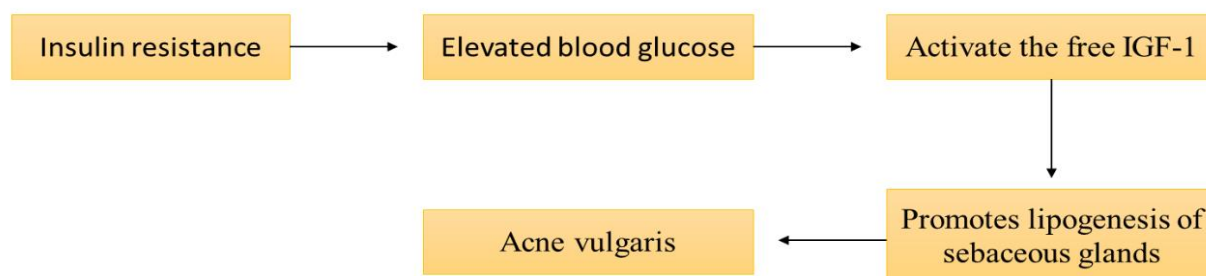
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**ABSTRACT****Figure 1:** Graphical Abstract

Acne vulgaris affects between 83-100% of adolescents at some time in their life. Insulin resistance plays an important role in acne vulgaris as elevated blood glucose levels in the disease activate the free IGF-1 which promotes lipogenesis of sebaceous glands thus leading to acne formation. The study was aimed to analyze the correlation between insulin resistance and the severity of acne vulgaris. A total of 100 patients clinically diagnosed with acne vulgaris were enrolled in the study. The severity of the acne was evaluated using the GAGS system. The HOMA-IR index was used for the analysis of insulin resistance. The mean age of the patients was 22.13 years with a predominance of females i.e., 76%. GAGS score revealed 89% of patients had mild acne, 9% of patients had moderate acne and 2% of patients had severe acne. As per the HOMA-IR index cutoff value of 2.5, 35% of patients in our study had insulin resistance. A significant positive correlation was observed between the acne vulgaris and insulin resistance. Early treatment of insulin resistance can help evaluate a patient's metabolic aspects that should be helpful in the diagnosis and treatment of various other skin conditions associated with it apart from acne vulgaris such as acanthosis nigricans, acrochordons, etc., and improving the health and the quality of care for these patients.

**Keywords:** Acne vulgaris, Insulin resistance, GAGS, HOMA-IR.**INTRODUCTION**

Acne vulgaris is a disease of the pilosebaceous unit. Depending upon the severity of the inflammatory process, it is characterized clinically by the formation of different types of skin lesions which includes comedones, papules, pustules, nodules, and cysts that are usually present on the background of oily skin<sup>[1]</sup>. It usually begins during puberty and tends to be more severe in males. Being largely an

adolescent condition, it may affect people of different ages, but it also has a significant psychological impact that can result in low self-esteem, social exclusion, and serious depression<sup>[2]</sup>.

Insulin resistance (IR) plays an important role in the onset of acne. In IR, tissues normally do not respond to the physiological actions of insulin, which results in elevated glucose level in blood. In response

to higher blood glucose levels, more insulin is produced by the pancreas i.e., Hyperinsulinemia to normalize the blood sugar. Hormone cascade thus initiated favors the tissue growth by activating the free Insulin-like Growth Factor-1 (IGF1) because free IGF1 promotes lipogenesis of sebaceous glands thus leading to acne formation [3-9].

Increased levels of insulin can produce hyperandrogenism in females with severe IR states by enhancing the pituitary response of Luteinizing Hormone (LH) to Gonadotropin Releasing Hormone (GnRH), thereby stimulating ovarian LH-mediated androgen production<sup>[10]</sup>. In males, hyperinsulinemia stimulates the synthesis of testosterone and inhibits the production of Sex Hormone-Binding Globulin (SHBG) at the hepatic level thereby increasing the bioavailability of androgens<sup>[11]</sup>.

Nevertheless, it is still difficult to diagnose acne in relation to IR. Numerous approaches, including the euglycemic metabolic clamp, the HOMA index, and the QUICKI, have been presented for IR assessment. Among all these, HOMA-index is the most frequently used method. GAGS and AFAST are two grading systems that may be used to determine the clinical severity of acne. There is yet no technique that can definitively diagnose both concurrent IR and acne in a single test<sup>[12]</sup>. The most recent research indicates that more than 85% of youngsters suffer from acne and that occasionally even the most advanced therapy techniques fail to provide relief. Additionally, several research initiatives have been devoted to the issue of reducing adverse events, but the problem of developing novel, tailored treatments for acne has remained unanswered. Because IR and acne share several pathogenic characteristics, effective IR treatment may also improve the clinical condition of acne<sup>[13]</sup>. This study was aimed to evaluate the association between insulin resistance and acne vulgaris and also to analyze the correlation of IR with the severity of acne vulgaris.

## MATERIALS AND METHODS

### Study design

Total 100 patients clinically diagnosed with acne vulgaris were included in the study. Patients on medications that can interfere with the normal metabolism of insulin such as corticosteroids, and oral contraceptive pills were excluded from the study. The study has been approved by the institute ethics committee of M. M. Medical College and Hospital under reference number MMMCH/21/435.

### Blood sample

A total of 5 ml peripheral venous blood sample was collected from each patient after 10 hrs of fasting. Fasting plasma glucose (74-106 mg/dl) was analyzed by the hexokinase method on the Siemens dimensions auto-analyzer. Fasting insulin (2-25 miu/l) was determined by the chemiluminescent immunoassay method on the Advia Centaur XP system.

### GAGS (Global Acne Grading System)

GAGS is a standardized method for assessing the severity of acne vulgaris. It provides a uniform approach to evaluating the number,

size, and type of acne lesions, which helps healthcare providers to determine the most appropriate treatment plan. The system considers various factors such as the number of inflammatory and non-inflammatory lesions (such as papules, pustules, and nodules), as well as the presence of scarring. A higher GAGS score indicates a more severe form of acne.

### HOMA-IR

HOMA-IR is a mathematical formula used to estimate insulin resistance in individuals. HOMA-IR was calculated based on the blood glucose and insulin level using the following formula:

$$HOMA - IR = \frac{Glucose \times Insulin}{405}$$

A HOMA-IR value of greater than 2.5 is commonly considered to indicate insulin resistance.

### Statistical Analysis

The statistical analysis was carried out using SPSS 27.0. For quantitative variables, mean was used as measures of central tendency. For qualitative variable, fraction of total was calculated. Pearson's correlation was used to analyze correlation between two variables. A p value <0.05 was considered as significant.

## RESULTS AND DISCUSSION

The age of the study subjects was between 12-40 years. The maximum number of patients i.e., 77, were in the age group of 21-30 years followed by 21 patients in the age group of 10-20 years and only 2 patients between 31- 40 years. The mean age of the patients was 22.13 years. The majority of patients i.e., 76, were females and rest of 24 patients. Total 88 patients were from urban areas whereas 12 patients were from rural areas. Maximum number of patients were students i.e., 88, followed by 6 patients were doing private jobs and 6 patients were housewives (Table 1).

**Table 1:** Sociodemographic determinants of the patients.

Variable	Subdomain	Number of patients
Age groups	12-20 years	21
	21-30 years	77
	31-40 years	2
Gender	Male	24
	Female	76
Locality	Rural	12
	Urban	88
Occupation	Student	88
	Private Job	6
	Housewife	6

GAGS score was used to assess the severity of acne. Our study observed that 89 patients had mild acne, 9 patients had moderate acne and 2 patients had severe acne. There were no patients with very severe acne (Table 2)

**Table 2:** GAGS scoring for severity of acne vulgaris.

GAGS Score	Number of patients
Mild (1-18)	89
Moderate (19-30)	9
Severe (31-38)	2
Very severe (>39)	0

The most commonly used index to assess IR is the HOMA index. We used 2.5 as the cut-off value and found out that 35 subjects had a value of >2.5 which indicate number of patients with insulin

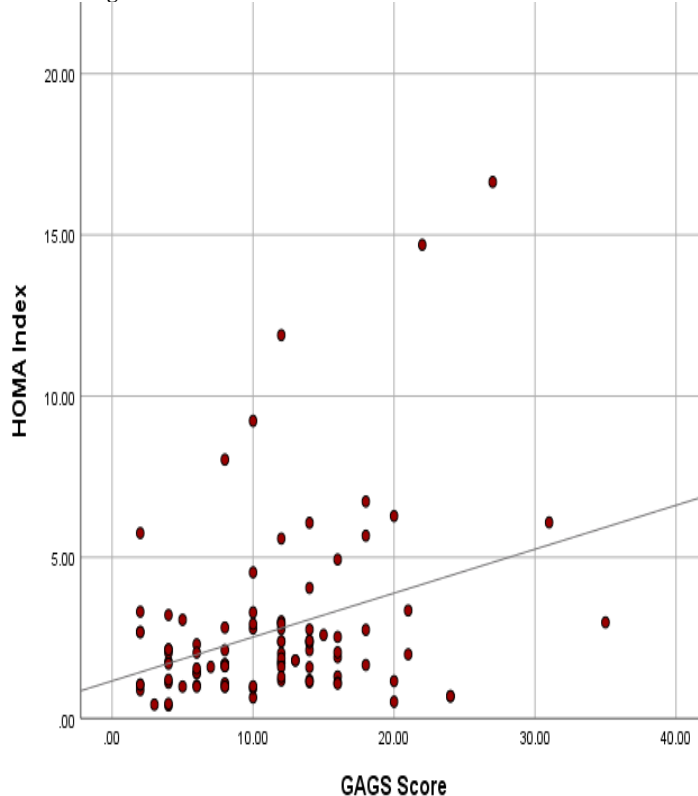
resistance (Table 3).

**Table 3:** HOMA-IR for analysis of insulin resistance.

HOMA-IR	Number of patients
HOMA-IR $\leq 2.5$	65
HOMA-IR $> 2.5$	35

A significant positive correlation ( $r=0.33$  and  $p=0.000^*$ ) was observed between the severity of acne according to GAGS scoring and insulin resistance indicated by HOMA-IR (Figure 1).

**Figure 2:** Correlation between the HOMA-IR and GAGS.



It is crucial to investigate the prevalence of illness of acne in hospitals while periodically evaluating the clinical profile and association with various pre-disposing factors. Such research is required to assess the clinical-epidemiological profile and etiopathogenesis. Therefore, we investigated the varied clinical manifestations of acne vulgaris in both sexes and throughout a range of age groups.

Doshi et al.(1997) was first to proposed the GAGS, a simplified tool used to measure acne grading<sup>[14]</sup>. In our study majority of the patients i.e., 89% belonged to the mild category. This was comparable to the study done by Hacivelioglu et al. (2013) where the majority i.e., 86 of the patients out of 133 had mild acne<sup>[15]</sup>. However, the study done by Munichandrapa et al. (2017) included 45 cases out of which 29 patients had moderate acne<sup>[16]</sup>. A study done by Sultana et al. (2017) saw that majority of patients i.e., 41.6% had moderate acne followed by 29.17% with mild acne and 12.5% with severe acne<sup>[17]</sup>. In our study majority of patients was female may be because acne is more prevalent in female due to complex hormonal physiology. Similar results were reported by the Munichandrapa et al. (2017) study in which out of 45 cases, 26 were females and 19 were males<sup>[16]</sup>.

In terms of IR diagnostics, the HOMA method is often one of the fundamental and widely used approaches, and our study has employed it as well. According to Geloneze et al. (2009), the cut-off values are over 2.7 HOMA1-IR and above 1.8 HOMA2-IR<sup>[18]</sup>. In recent Brazilian research, the cut-off value for HOMA-IR was established at 2.7, the same number as the Turkish Metabolic Syndrome Guides approve<sup>[19, 20]</sup>. In our study, 35 participants had a value greater than 2.5 when we selected 2.5 as the cut-off threshold. We based our cut-off value of 2.5 on a prior Indian study that showed that according to ATP III and IDF criteria, a HOMA-IR cut-off of 2.5 had the highest sensitivity (more than 70%) and specificity (more than 60%) for identifying metabolic syndromes in both sexes<sup>[21]</sup>. Munichandrapa et al. (2017) did a case-control study and observed no statistically significant difference in mean HOMA IR in both these groups<sup>[16]</sup>.

The study conducted by Emiroğlu et al. (2015) found a significant difference in HOMA index value between the patients and control groups i.e. ( $p < 0.001$ )<sup>[22]</sup>. A study done by Tsai et al. (2020) found that on comparing the HOMA IR in patients with acne with controls, a higher incidence was found in the study group and this was found to be statistically significant but was contrasting to our study<sup>[23]</sup>. The reason that the majority of the study participants had normal HOMA index levels was attributed to the fact that most of the participants showed normal levels of fasting insulin and fasting glucose. Thus, fewer patients showed insulin resistance.

The present study found a significant correlation between the severity of acne according to GAGS scoring and insulin resistance as indicated by the HOMA index. Similarly, to this, Soodan et al. (2021) used 2.5 as the cut-off threshold in their research<sup>[24]</sup>. Both males and females with grade IV acne had higher mean HOMA-IR values. It was shown that the HOMA-IR value rose with the severity of acne, indicating that insulin resistance had a favourable correlation with acne severity. In their investigation, there was no discernible difference in HOMA-IR between males and females<sup>[24]</sup>. Similar findings were obtained in the research of Munichandrapa et al (2017), the mean HOMA-IR of patients and controls did not differ in a statistically significant way<sup>[16]</sup>. Balta et al. (2015) also reported the similar results<sup>[25]</sup>. However, research by Nagpal et al. (2016) revealed noticeably higher HOMA-IR levels in acne patients compared to controls<sup>[26]</sup>. Early detection of insulin resistance may aid in better managing acne patients because acne is an issue in adolescents.

## CONCLUSION

Dermatologists should be aware of the possible connection between IR and acne, and they should think about sending acne patients to primary care for further testing. In the present study, we observed that 89% of patients had mild acne, only 9% of patients had moderate acne, and 2% of patients had severe acne. At the HOMA index cut-off of 2.5, 35% of patients exhibited insulin resistance. The severity of acne

according to GAGS scoring correlated well with the rise in HOMA-IR. Early treatment of insulin resistance can help evaluate a patient's metabolic aspects that should be helpful in the diagnosis and treatment of various other skin conditions associated with it apart from acne vulgaris such as acanthosis nigricans, acrochordons, etc., and improving the health and the quality of care for these patients.

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