ACNE AND INSULIN RESISTANCE: A SYSTEMATIC REVIEW
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ABSTRACT
Acne is a skin disorder that is characterized by persistent inflammation and involves the folliculopilosebaceous unit. It has an impact on a sizeable portion of the general population. Acne affects a disproportionate number of females and teenagers, especially those between the ages of 15 and 24, who are most susceptible to the condition. In recent times, there has been seen to be a growing interest in the possible connection between acne and insulin resistance (IR). This attention has been seen, and it is appreciated. It would appear that IR has a strong connection to acne, which is a persistent skin condition that can lead to inflammation. Research has been conducted on a wide variety of etiopathological factors that have been associated with the progression of IR. It would appear that obesity is one of the most common. Additionally, it would appear that factors such as chronic inflammation, hypertriglyceridemia, low HDL serum concentration, mitochondrial dysfunction, gut microbiota, and the excess activity of antagonistic hormones such as cortisol, glucagon, and thyroid hormones all play a significant role in the development of this condition. We identified a linkage between insulin resistance and severe acne vulgaris, which was reported to have a positive link with insulin resistance. On the basis of these findings, it is a legitimate assumption to hypothesize that medications that are now utilized for the treatment of insulin resistance would also be helpful for the treatment of severe acne vulgaris.

Keyword: Acne; Glucose; Inflammation; Insulin resistance
INTRODUCTION
Acne is a chronic inflammatory skin disease that involves the folliculopilosebaceous unit. It affects a reasonably large number of people. Acne affects a disproportionate number of females and teenagers, particularly those between the ages of 15 and 24. Lesions of the skin, including comedones, papules, pustules, and nodules, are typically found deep beneath the skin of the face, shoulders, back, and chest. Acne, a common skin condition, is ranked on a severity scale from mild to severe. Mild acne is the least severe form, while severe acne is the most severe.1–3

Acne is a condition that can manifest in a variety of different ways and has a highly complicated etiopathology. It is characterized by an overabundance of sebum production, also known as hyperseborrhea, as well as inflammation. There are a number of transcription factors that are associated with sebum production, including forkhead box protein O1 (FoxO1), 1,25-dihydroxyvitamin D, and calcium.3–5

Recently, there has been observed an increasing interest in the potential association between acne and insulin resistance (IR). This interest has been observed. Acne, which is a chronic skin disorder that causes inflammation, appears to have a strong link to IR.1 The IR evaluation seems to be of utmost importance both in the process of detecting this condition and in the process of formulating a treatment plan for it. Both conditions are characterized by the presence of similar signal transduction pathways, namely mammalian target of rapamycin kinase 1 (mTORC1) and insulin-like growth factor-1 (IGF-1).4

Despite this, determining whether acne is caused by IR continues to be a difficult diagnostic task. IR can be evaluated using a variety of methods, some of which include the euglycemic metabolic clamp, the Homeostasis Model Assessment (HOMA-index), and the Quantitative Insulin Sensitivity Check Index (QUICKI).6 The clinical severity of acne can be measured using scoring methods like the Global Acne Grading System (GAGS) or the Adult Female Acne Scoring Tool (AFAST). However, there is not yet a procedure that can provide a definitive diagnosis of coexisting acne and IR by the use of a single test.7,8

The objective of this piece is to investigate the possible connection between acne and insulin resistance.

METHODS
The full-text papers written in English were used as the source material for the data that was gathered for the purpose of conducting this systematic review. The review's purpose was to determine association between acne and insulin resistance (IR). During the process of producing this essay, the databases Pubmed and Google Scholar were utilized extensively throughout the research phase. The following was mentioned among the conditions for eligibility: (1) A cohort study, cross-sectional study, or case–control study that reported the risk of insulin resistance among patients with acne compared with participants who did not have acne; (2) A relative risk, hazard ratio, incidence ratio (IR), or standardized IR with 95% confidence intervals (CIs), or sufficient data to calculate those ratios were provided.

The keywords used in the search were “acne” and “insulin resistance”. We include study conducted above in 2012–2022. This analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) paradigm, in which the researchers originally entered keywords into each database. The phrases: (“insulin resistance”[MeSH Terms] OR (“insulin”[All Fields] AND "resistance"[All Fields]) OR "insulin resistance”[All Fields]) AND (“acne vulgaris”[MeSH Terms] OR (“acne”[All Fields] AND "vulgaris"[All Fields]) OR "acne vulgaris”[All Fields] OR "acne”[All Fields]) used in this study. We received four articles, which will be discussed during the discussion (Table 1).

RESULT
First study showed glycemic index and glycemic load levels were significantly higher (P = .022 and P = .001, respectively) and serum adiponectin levels were significantly lower (P = .015) in patients with acne than in the control subjects. There was an inverse correlation between serum adiponectin concentration and glycemic index (P = .049, r = −0.212). Acne vulgaris was found to have a favorable correlation with a diet high in glycemic index and load. There is a possibility that adiponectin is a pathogenetic cofactor that contributes to the progression of the disease. In order to fully understand the nature of this potential connection, it will be necessary to do additional studies on the levels of adiponectin that are present in acne patients who have developed insulin resistance.9
Table 1. The literature include in this study

<table>
<thead>
<tr>
<th>Author</th>
<th>Origin</th>
<th>Method</th>
<th>Sample Size</th>
<th>Index</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerman, 2016</td>
<td>Turkey</td>
<td>Cross sectional</td>
<td>Patient: 243</td>
<td>BMI, Glucose, Insulin, HOMA</td>
<td>Glycemic index and glycemic load levels were significantly higher ($P = .022$ and $P = .001$, respectively) and serum adiponectin levels were significantly lower ($P = .015$) in patients with acne than in the control subjects. There was an inverse correlation between serum adiponectin concentration and glycemic index ($P = .049$, $r = -0.212$).</td>
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<tr>
<td>Emiroglu, 2015</td>
<td>Turkey</td>
<td>Cross sectional</td>
<td>Patient: 50</td>
<td>BMI, Glucose, Insulin, HOMA</td>
<td>All of the patients were in the severe acne group according to their scores on the global acne scoring scale. While fasting blood glucose levels were not different between the groups ($p &gt; 0.05$, 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 ($p &lt; 0.001$, 14.01 ±11.94 vs. 9.12 ±3.53). Additionally, there was a highly significant difference between the patient and control groups in terms of HOMA values ($p &lt; 0.001$, 2.87 ±2.56 vs. 1.63 ±0.65).</td>
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<tr>
<td>Nagpal, 2016</td>
<td>India</td>
<td>Cross sectional</td>
<td>Patient: 100</td>
<td>BMI, Glucose, Insulin, HOMA</td>
<td>According to the findings presented by Nagpal, the prevalence of insulin resistance was found to be substantially greater in cases (22%) than in controls (11%) ($P = .03$). There was no significant difference in the prevalence of metabolic syndrome between the cases (17%) and the controls (9%) ($P = .09$). It was shown that there was no significant difference in the prevalence of insulin resistance or metabolic syndrome between the acne severity groups.</td>
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<tr>
<td>Del Prete, 2012</td>
<td>Italy</td>
<td>Cross sectional</td>
<td>Patient: 22</td>
<td>BMI, Glucose, Insulin, HOMA</td>
<td>The results thus obtained are as follows, patients had higher BMI ($p = 0.003$), WC ($p = 0.002$), WHR ($p = 0.02$), SBP ($p = 0.0001$), DBP ($p = 0.001$), basal ($p = 0.1$) and 120 min. oGTT serum insulin concentrations ($p = 0.002$), basal glucose concentrations ($p = 0.03$), HOMA-IR ($p = 0.016$), and lower HDL-cholesterol than controls ($p = 0.001$). Among the subgroup of subjects with BMI &lt;24.9, HDL-cholesterol ($p = 0.05$) and 120 min. oGTT serum insulin concentrations ($p = 0.009$) resulted to be independent predictors of acne at multivariate analysis. In conclusion, these findings highlight a metabolic imbalance in young males affected with acne. Insulin resistance seems to play the main role for the development of acne in these subjects. Insulin resistance could represent an effective target for therapy in male acne.</td>
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A common finding of acne in women with polycystic ovarian syndrome, an endocrinologic abnormality in which insulin resistance may be causal for development of acne, prompted a cross-sectional study to identify the prevalence of insulin resistance and metabolic syndrome in male patients 20 years of age or older with acne. Nagpal study aimed to identify the prevalence of insulin resistance and metabolic syndrome in male patients with acne. Prevalence of insulin resistance was found to be substantially greater in cases (22%) than in controls (11%) (P =.03). There was no significant difference in the prevalence of metabolic syndrome between the cases (17%) and the controls (9%) (P =.09). It was shown that there was no significant difference in the prevalence of insulin resistance or metabolic syndrome between the acne severity groups. The results thus obtained are as follows, patients had higher BMI (p = 0.003), WC (p = 0.002), WHR (p = 0.02), SBP (p = 0.0001), DBP (p = 0.001), basal (p = 0.01) and 120 min. oGTT serum insulin concentrations (p = 0.002), basal glucose concentrations (p = 0.03), HOMA-IR (p = 0.016), and lower HDL-cholesterol than controls (p = 0.001). Among the subgroup of subjects with BMI <24.9, HDL-cholesterol (p = 0.05) and 120 min. oGTT serum insulin concentrations (p = 0.009) resulted to be independent predictors of acne at multivariate analysis. In conclusion, these findings highlight a metabolic imbalance in young males affected with acne. Insulin resistance seems to play the main role for the development of acne in these subjects. Insulin resistance could represent an effective target for therapy in male acne.

DISCUSSION

Despite normal or increased insulin secretion, insulin resistance (IR) is described as a failure of insulin to enable optimal glucose transport into metabolic tissues such as skeletal muscle, adipose tissue, and liver. This can occur even when insulin levels are normal. IR is the cause of the development of hyperglycemia as well as hyperinsulinemia, which are both consequences of the condition. Both genetic and environmental variables have been implicated in the development of IR. There have been numerous genetic loci found that have been linked to an elevated risk of IR up until this point. Also included in this category are those linked to glucose metabolism, insulin actions, signaling in insulin-dependent tissues, or the activation of insulin and IGF receptors.

![Figure 1. Article search flowchart](image-url)
There has been research done on a diverse range of etiopathological variables that have been linked to the development of IR. It would appear that obesity is one of the most prevalent. In addition, it appears that factors such as chronic inflammation, hypertriglyceridemia, low HDL serum concentration, mitochondrial dysfunction, gut microbiota, and the excess activity of antagonistic hormones such as cortisol, glucagon, and thyroid hormones all play a significant role. Certain lifestyle choices, such as smoking, consuming a large amount of milk and carbs, and running a high risk of developing insulin resistance and hyperinsulinemia are all linked together.

IR is a risk factor in its own right for cardiovascular illnesses, type 2 diabetes, and non-alcoholic fatty liver disease, in addition to being a component of the metabolic syndrome. It is possible for this condition to coexist with decreased glucose tolerance as well as hypertension. IR is also linked to a wide range of endocrine conditions, including but not limited to acromegaly, hyperprolactinemia, hypercortisolism, hypopituitarism, hyper- and hypothyroidism, primary hyperparathyroidism, pheochromocytoma, primary aldosteronism, congenital adrenal hyperplasia (CAH), polycystic ovary syndrome (PCOS), and hypogonadism.

Figure 2. Comparison of patient and control insulin by study

Figure 3. Comparison of patient and control HOMA by study
As was just noted, acne seems to have a substantial association with IR, although the role that IR plays in the etiology of acne is not yet fully understood. The production and secretion of insulin are both stimulated by high glycemia, which in turn increases the production of androgens by the ovaries and adrenal glands. It is also possible for it to diminish the blood level of sex hormone-binding globulin (SHBG), which will severely amplify androgen activity and make it easier for acne to develop. Insulin lowers the amount of IGF-1 binding protein in the body, which results in a considerable increase in the quantity of free IGF-1 in the blood. Smith et al. have shown that IGF-1 stimulates lipogenesis in SEB-1 sebocytes by activating the Phosphoinositide 3-kinase (PI3-K)/Akt pathway.

This activation of these pathways results in an increase in the expression of sterol regulatory element-binding protein-1 (SREBP-1), which in turn stimulates lipogenesis. Increased mTORC1 activity, which is closely connected with insulin resistance, obesity, type 2 diabetes, and several malignancies such as melanoma and prostate cancer, has been identified in people who suffer from acne. It would appear that IR is generated by phosphorylation of the insulin receptor substrate-1, which is caused by the activation of S6K1 kinase in response to an increase in the activity of mTORC1. Additionally, a substantial association between a lower expression of insulin, IGF-1, and mTORC1 and a lower prevalence rate of acne has been identified. This correlation has been observed to be statistically significant.

In the case of young guys, IR has been reported in the literature as being present throughout the duration of acne. The researchers Nagpal and colleagues found a strong association between the HOMA-IR value and the progression of acne. However, there was not a statistically significant difference seen between the HOMA-IR score, metabolic syndrome, and acne severity. Del Prete et al. on the male population of acne sufferers, a significant correlation was found to exist.
between the acne score and HOMA-IR. This correlation was found to exist despite the exclusion of any potential influence from an abnormal androgenic profile.\textsuperscript{12,20}

The abnormal androgenic profile was evaluated based on measurements of serum levels of free testosterone, total testosterone, dehydroepiandrosterone sulfate (DHEAS), and SHBG. Therefore, it has been determined that hyperinsulinaemia, and not increased androgen activity, may have been the sole factor responsible for acne's development.\textsuperscript{12} According to research carried out by Kartal and colleagues, IR is a risk factor for acne that exists independently of hyperandrogenemia as well.\textsuperscript{21} Emiroglu et al.\textsuperscript{10} obtained the results of a much higher HOMA value in both male and female acne patients (HOMA = 2.87), and the value indicated that the IR had already established. whereas Cerman and colleagues showed that acne sufferers had lower levels of adiponectin.\textsuperscript{9}

**CONCLUSION**

Insulin resistance was reported to have a positive link with severe acne vulgaris, and we found this correlation. Based on these data, it seems reasonable to hypothesize that therapies now used for insulin resistance would also be effective for the treatment of severe acne vulgaris.

**REFERENCE**