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The relationship between acne vulgaris and insulin resistance in adolescents

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Abstract
Background: Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit that usually affects adolescents. The aetiology and severity of acne may be influenced by hyperinsulinemia and insulin resistance.
Aim: The present study was aimed at determining the association between insulin resistance and the development of acne vulgaris.
Patients and Methods: This case-control study conducted at Salah Aldin General Hospital from September 1, 2023, to the end of March 2024 included 80 patients diagnosed with acne vulgaris (45 males and 35 females) and 80 healthy controls (45 males and 35 females), aged between 10 to 19 years. Informed consent was obtained from all participants. The inclusion criteria comprised individuals with acne vulgaris aged 10 to 19 years, including both males and females. Exclusion criteria involved hormonal disorders, hormonal treatment, chronic diseases, and high consumption of specific food items. Acne severity was classified based on the American Academy of Dermatology Acne Consensus. Data collection involved questionnaires, physical examinations, and laboratory assessments. Laboratory assessments included the collection of venous blood samples from patients and controls after an overnight fast. Serum insulin and C-peptide levels were determined using ELISA, while blood sugar levels were assessed through biochemical colorimetric methods. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using a specific formula.
Results: The study compared various metabolic parameters between acne patients and a control group, revealing significant differences. Acne patients exhibited higher mean levels of RBS (6.16±0.89 mmol/L) and C-Peptide (3.98±0.17 ng/mL) compared to the control group (RBS: 5.43±0.98 mmol/L; C-Peptide: 0.92±0.11 ng/mL), with corresponding p-values of 0.032 and 0.001 respectively. Conversely, acne patients showed lower insulin levels and higher HOMA-IR values compared to the control group. The study found a significant association between acne and insulin resistance, with 31.25% of acne patients testing positive for insulin resistance compared to none in the control group. Additionally, the severity of acne, as classified by the Voulgaris classification, showed that 21.25% had mild acne, 45.00% had moderate acne, and 33.75% had severe acne. The predominant site of acne lesions was the face (76.25%), with combinations across multiple areas observed. Age and sex were found to be associated with acne severity, with older age groups and males showing a higher prevalence of severe acne. Furthermore, a significant relationship was observed between insulin resistance and age among acne patients, with higher HOMA-IR levels associated with older age groups. Sex-based differences were also noted, with males exhibiting lower mean HOMA-IR levels compared to females. These findings highlight the intricate interplay between metabolic factors, acne severity, age, and sex in individuals with acne, underscoring the importance of considering these factors in acne management and treatment strategies.

Keywords: Acne vulgaris, insulin resistance, adolescents

1. Introduction
Acne vulgaris is a very common skin disorder and its prevalence is still increasing. The first symptoms usually occur at the age of 11–12 years old and, eventually, up to 85% of adolescents are affected. Acne vulgaris is a growing problem in developed countries and is rare in developing countries. The reason for the lower incidence of acne lesions in patients from less affluent countries is a diet containing less milk and fewer dairy products and carbohydrates [1]. Western diets, which contain food with a high glycemic index, have a significant impact in terms of disturbances in glucose and insulin serum levels and are associated with the development of insulin resistance (IR) [2].

In severe cases, acne may have an impact on skin condition in adulthood, especially when severe lesions do not heal properly, leading to discolorations and scars. The number of adult patients with acne vulgaris continues to increase. Moreover, both acne and its complications may reduce self-confidence and induce mental health problems [1]. It is worth highlighting that the occurrence of extensive acne lesions affects the quality of life and is a factor that influences psychosociological health. The correlation between psychosocial disorder and acne vulgaris is more significant among women than in the male population [3].

The development of acne lesions is strongly associated with metabolic and hormonal disorders. Acne vulgaris may be induced in the course of disorders that are characterized by abnormal levels, not only of androgens, estrogens, and progesterone but also of insulin and insulin-like growth factor-1 [4]. Acne vulgaris may be regarded as a civilization-related disease, as is IR. The skin often reflects the body's internal health; therefore, acne formation may be associated with IR. IR is a condition characterized by the failure of insulin to provide the proper glucose transport from the bloodstream into the tissues, which results in the development of hyperglycemia and hyperinsulinemia [6].

Recently, a growing level of interest concerning a possible relationship between these diseases has been observed, although thus far, little information is available. What is already clear is that insulin serum levels have been observed to be elevated in patients with acne vulgaris, and that both acne and IR share the hormonal and signal transduction pathways, including insulin-like growth factor-1 (IGF-1) and the mammalian target of rapamycin kinase 1 (mTORC1) [7]. Furthermore, both acne and IR are observed in the course of syndromes such as HAIR-AN or hyperandrogenism (HA), IR, and acanthosis nigricans (AN) or polycystic ovary syndrome (PCOS) [8]. Several studies have revealed noticeably higher insulin serum levels and HOMA values among acne patients compared to the healthy controls; therefore, they indicate the importance of considering IR as a causative factor in acne formation [9, 10, 11]. However, as yet, no research has been conducted on the Polish population and more data are required in order to include IR evaluation as part of standard acne diagnostics and treatment options.

2. Patients and Methods

2.1 Patients

The study included 80 participants (80 patients diagnosed with acne vulgaris (45 males and 35 females) and 80 healthy control individuals (45 males and 35 females)) with age range between 10-19 years (mean: 14.5 for patients and 15.1 years for the control group) . Informed consent was obtained from each participant.

2.2 Methods

2.2.1 Classification of acne severity

The classification of acne severity has been developed by the American Academy of Dermatology Acne Consensus Conference (ACC). This classification was based on the number and type of lesion present. According to this classification, the patient group was divided into three subgroups:

1. **Mild:** Patients exhibit few to several papules and pustules without any nodules.
2. **Moderate:** Patients present with several to many papules, pustules, and a few nodules.
3. **Severe:** Patients have many to extensive papules and pustules lesions with numerous nodules.

2.2.2 Data collection

Subjects were asked to complete a questionnaire, after which, a physical examination was performed. The severity of the patient's acne was evaluated using the investigator's global assessment scale. A physical examination was performed in the control group.

2.2.3 Laboratory assessments

Five ml of venous blood was collected by vein puncture 5 ml syringes from each patient and control enrolled in this study in fating status. Blood samples were placed into test tubes, the tube then were centrifuged (3000 rpm) for 15 min. The clear serum was pipetted into clear dry Eppendorf's tubes and stored at (-20°C) for determination of serum insulin and C-peptide by ELISA and blood sugar by biochemical colorimetric. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the formula: (fasting insulin serum level × fasting glucose serum level) / 22.5.

3. Results

3.1 A comparative analysis of insulin resistance parameters between acne patients and the control group

The study showed that acne adolescent exhibited a higher mean of RBS (6.16±0.89 mmol/L), while the control group showed a slightly lower mean level (5.43±0.98 mmol/L). This difference was found to be statistically significant with a p-value of 0.032. Regarding C-Peptide levels, acne patients demonstrated a markedly higher mean level of 3.98±0.17 ng/mL compared to the control group's mean of 0.92±0.11 ng/mL, indicating significantly elevated C-Peptide levels in acne patients (p-value = 0.001). Additionally, acne patients had lower insulin levels, with a mean of 5.84±0.95 µU/mL, compared to the control group's higher mean of 7.31±1.81 µU/mL. The analysis of HOMA-IR values also revealed a significant disparity between the two groups, with acne patients having a mean HOMA-IR of 1.93±0.56, while the control group had a lower mean of 1.48±0.39.

Table 1: A comparative analysis of insulin resistance parameters between acne patients and the control group

Insulin IR Parameters	Studied groups	Mean±SD	P-value (significant)
RBS (mmol/L)	Acne	6.16±0.89	0.032
	Control	5.43±0.98	
C-Peptide (ng/mL)	Acne	3.98±0.17	0.001
	Control	0.92±0.11	
Insulin (µU/mL)	Acne	5.84±0.95	0.048
	Control	7.31±1.81	
HOMA-IR	Acne	1.93±0.56	0.015
	Control	1.48±0.39	

3.2 Prevalence of IR in acne patients and control group

The study findings indicate that, among the acne patients, 31.25% (25 out of 80) tested positive for insulin resistance, while 68.75% (55 out of 80) tested negative. In contrast, none of the individuals in the control group (0 out of 80) tested positive for insulin resistance, with 100% (80 out of 80) testing negative. This data suggests a significant association between acne and insulin resistance, with a

higher prevalence of IR observed among acne patients in comparison to the control group

Table 1: Prevalence of IR in acne patients and control group

HOMA IR	Acne patients		Control group	
	No.	%	No.	%
Positive	25	31.25%	0	0%
Negative	55	68.75%	80	100%
Total	80	100%	80	100%

P-value:0.001

3.3 Distribution of patients according to the severity of acne Voulgaris

The distribution of patients according to the severity of acne, as categorized by the Voulgaris classification, is presented in Table 4.2. The severity levels are delineated into mild, moderate, and severe categories. Among the patients surveyed, 21.25% were classified as having mild acne, representing 17 individuals. Moderate acne was observed in 45.00% of the patients, corresponding to 36 individuals. Meanwhile, severe acne accounted for 33.75% of the patients, encompassing 27 individuals.

Table 3: Distribution of patients according to the severity of acne Voulgaris

Acne severity	%	No.
Mild	17	21.25%
Moderate	36	45.00%
Severe	27	33.75%

3.4 The distribution of acne vulgaris lesions across different body parts

The distribution of acne vulgaris lesions across different body parts within the studied group reveals significant findings. The face stands out as the predominant site, with 61 cases, constituting 76.25% of the total. This high number underscores the primary manifestation of acne on the face. Additionally, combinations of acne across multiple areas are observed, such as the face and shoulders in 5 cases (6.25%), back and shoulders in 4 cases (5.0%), and face, back, and chest in 2 cases each (2.5%). Table 4.

Table 4: The distribution of acne vulgaris lesions across different body parts

Parts	No.	%
Face	61	76.25%
Face and shoulders	5	6.25%
Back and shoulders	4	5.0%
Back	2	2.5%
Chest	2	2.5%
Face, back, and chest	2	2.5%
Face, back, and shoulders	2	2.5%
Face and back	2	2.5%
Total	80	100%

3.5 Association between age groups, sex, and the severity of acne among the studied adolescents

The data reveals significant associations between age groups, sex, and the severity of acne among the studied population. Analysis of age groups indicates a progressive increase in acne severity with advancing age, with 66.67% of individuals aged 10-12, 25.93% of those aged 13-15, and merely 7.41% of individuals aged 16-19 exhibiting severe acne. Additionally, a substantial difference in acne severity emerges, with 70.37% of males exhibiting severe acne compared to 29.63% of females, Table 4.5

Table 2. Association between age groups, sex, and the severity of acne among the studied adolescents

Age groups	Acne patients						P-value
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
10-12	6	35.29%	15	41.67%	18	66.67%	0.048
13-15	6	35.29%	14	38.89%	7	25.93%	
16-19	5	29.41%	7	19.44%	2	7.41%	
Total	17	100%	36	100%	27	100%	
Sex							
Males	8	47.06%	18	50%	19	70.37%	0.049
Females	9	52.94%	18	50%	8	29.63%	
Total	17	100%	36	100%	27	100%	

3.6 Association between insulin resistance and age of acne patients

The study showed a statistically significant association between insulin resistance and the age of acne patients. Among those tested positive for insulin resistance, the mean age was 17.14 years, while among those tested negative, the mean age was notably lower at 13.76 years (p-value: 0.001).

Table 6: Association between insulin resistance and age of acne patients

HOMA-IR result	Age (years) Mean±SD
Positive (n:25)	17.14±3.56
Negative (n:55)	13.76±2.67

P-value: 0.001

3.7 Relationship between acne severity and insulin resistance

The study investigated the relationship between acne severity and insulin resistance, as measured by HOMA-IR levels. The results revealed varying HOMA-IR levels across different acne severity categories: mild, moderate, and severe. Among patients with mild acne, the mean HOMA-IR level was 15.7±0.81, while among those with moderate acne, it was 1.68±1.13, and among those with severe acne, it was notably higher at 2.09±1.26, Table 4.6.

Table 7: Relationship between acne severity and insulin resistance

Acne severity	No.	HOMA-IR	P-value *
Mild	17	15.7±0.81	0.001
Moderate	36	1.68±1.13	
Severe	27	2.09±1.26	

* P-value was calculated by Analysis of Variance (ANOVA)

3.8 Relationship between sex and insulin resistance

The study investigated the relationship between sex and insulin resistance, as indicated by HOMA-IR levels, among acne patients. Among the male participants (n=45), the mean HOMA-IR level was 1.69±0.57, while among the female participants (n=35), it was slightly higher at 1.82±0.54. A statistically significant difference in HOMA-IR levels between males and females was observed (p-value = 0.011).

This suggests a potential sex-based disparity in insulin resistance among individuals with acne, with males exhibiting lower mean HOMA-IR levels compared to females.

Table 9: Relationship between sex and insulin resistance

Sex	No.	HOMA-IR	P-value
Males	45	1.69±0.57	0.011
Females	35	1.82±0.54	

4. Discussion

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit that usually affects adolescents. The aetiology and severity of acne may be influenced by hyperinsulinemia and insulin resistance [1]. Insulin resistance has been found to be a strong predictor of metabolic illnesses in adults and the main component of metabolic syndrome. This has led to a new focus on research in this area [2, 3]. Here, in our study, we used HOMA-IR index for evaluating insulin resistance. The HOMA-IR index has been an accepted formula for measuring insulin resistance since 1985 [12]. Methods such as fasting insulin level, fasting glucose/insulin ratio, HOMA-IR and quantitative insulin-sensitivity check index are suggested to be used in population studies. HOMA-IR is a frequently used parameter in clinical research [13].

The study compared various metabolic parameters between acne patients and a control group, revealing significant differences. Acne patients exhibited higher mean levels of RBS (6.16±0.89 mmol/L) and C-Peptide (3.98±0.17 ng/mL) compared to the control group (RBS: 5.43±0.98 mmol/L; C-Peptide: 0.92±0.11 ng/mL), with corresponding p-values of 0.032 and 0.001 respectively. Conversely, acne patients showed lower insulin levels and higher HOMA-IR values compared to the control group. C-peptide is a product of pro-insulin derived during insulin synthesis that roughly represents the amount of insulin produced and released. C-peptide is a biologically active molecule that can also be used as a diagnostic biomarker [14]. C-peptide is considered a powerful indicator of metabolic syndrome, emphasizing the importance of this biomolecule in metabolic syndrome diagnosis. On the other hand, the logarithmized product of fasting triglycerides and fasting glucose levels (TyG) index is a surrogate for estimating insulin resistance compared to the HOMA-IR index because the insulin test is expensive and not available in most laboratories, especially in undeveloped countries [15].

The study found a significant association between acne and insulin resistance, with 31.25% of acne patients testing positive for insulin resistance compared to none in the control group. Additionally, the severity of acne, as classified by the Voulgaris classification, showed that 21.25% had mild acne, 45.00% had moderate acne, and 33.75% had severe acne. The predominant site of acne lesions was the face (76.25%), with combinations across multiple areas observed. Age and sex were found to be associated with acne severity, with older age groups and males showing a higher prevalence of severe acne. Furthermore, a significant relationship was observed between insulin resistance and age among acne patients, with higher HOMA-IR levels associated with older age groups. Sex-based differences were also noted, with males exhibiting lower mean HOMA-IR levels compared to females. These findings highlight the intricate interplay between metabolic factors, acne severity, age, and sex in individuals with acne, underscoring the importance of considering these factors in acne management and treatment strategies.

Firstly, acne patients exhibited higher mean levels of RBS and C-Peptide compared to the control group, indicating potential dysregulation in glucose metabolism among individuals with acne. These findings suggest a possible association between acne and insulin resistance, as evidenced by lower insulin levels and higher HOMA-IR values in acne patients. Remarkably, a substantial proportion of acne patients tested positive for insulin resistance, highlighting the clinical relevance of metabolic dysfunction in acne pathogenesis. This indicates that insulin resistance is not a universal phenomenon among acne patients but is present in a significant proportion. The association between insulin resistance (IR) and the development of acne vulgaris has been a topic of interest for various researchers, and the findings in the current study align with those of previous investigations. Monica Singh *et al*. conducted a study involving 80 acne patients and 80 healthy controls, revealing statistically higher mean Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) values in the acne group compared to the controls. Notably, no correlation was identified between HOMA-IR and the severity of acne in this study [16].

In agreement with the current finding, Sharma *et al*. [17] examined a mixed-sex cohort of 100 adult patients and 100 controls, finding a statistically higher mean HOMA-IR value in the acne group compared to the control group Similarly, Mustafa *et al*. [18] demonstrated the impact of insulin resistance on acne vulgaris formation. In a mixed-sex group of 60 acne patients, the median HOMA-IR value was statistically higher than in an identical non-acne group. The insulin serum level was lower in acne patients compared to controls, and it negatively correlated with acne severity [1, 4, 5]. In line with our findings, Soodan *et al*. [19] discovered that out of a total of 500 participants, the mean HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) was higher in patients with acne as compared with the control individuals.

In line with our finding, Nagpal *et al*. [20] conducted a study with 100 male patients and 100 controls, revealing statistically higher mean HOMA-IR values in the acne group (compared to non-acne controls, while ruling out any potential impact of hyperandrogenemia. Furthermore, other studies, including those by Nurhadi *et al*. [21], Andreadi *et al*. [22], and Del Prete *et al*. [23] reported statistically higher mean HOMA-IR values in case group compared to control groups. However, Greabu *et al*. [24] did not observe any significant connection between insulin resistance and the formation of acne vulgaris.

In the current study, males exhibited high prevalence rates of severe acne infection as compared with females. Similar other studies, including those by Nurhadi *et al*. [16], Andreadi *et al*. [25], and Del Prete and colleagues [26] also reported agreed finding. significant gender-based difference in the severity of acne underscores the heightened prevalence of severe acne among males, highlighting a potential gender-specific aspect to the manifestation of acne [27]. In agreement with our findings, Soodan and colleagues [18] discovered that out of a total of 500 participants, 262 (52.4%) were males, and 238 (47.6%) were females. The average age of the study group was 21.63 years. The mean HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) was higher in individuals with grade IV acne, additionally, there was a positive correlation observed between fasting insulin levels

and HOMA-IR values, particularly in subjects with more severe acne.

In the present study, significant differences were observed in glucose levels (mmol/L), insulin levels and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) across varying degrees of acne severity. A study done by Adebamowo *et al*. showed the high higher HOMA index results and reported that hyperinsulinemia in patients with acne [28]. Furthermore, a more recent systematic review and meta-analysis by Nickles *et al*. found that severe acne patients had a higher HOMA index, indicating greater insulin resistance, than mild and moderate ones (P = 0.01) [29]. According to the local literature about the relationship between metabolic disorders and acne vulgaris, a recent study conducted in the same center also showed a significant association and positive correlation between the development of acne and the severity of acne with the level of higher HOMA index, which reinforce the current research finding and link the possibility of metabolic derangement as a cause of acne and a risk factor for its severity [30].

5. Conclusions

1. Acne patients exhibited significantly higher levels of random blood sugar (RBS), C-peptide, and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) compared to the control group.
2. The prevalence of insulin resistance was notably higher among acne patients, with 31.25% testing positive compared to none in the control group, indicating a significant association between acne and insulin resistance.
3. The severity of acne, as categorized by the Voulgaris classification, showed a substantial proportion of patients with moderate and severe acne, indicating the clinical significance of acne severity assessment.
4. Acne vulgaris lesions predominantly manifested on the face, with significant associations observed between acne severity, age, and sex, with older individuals and males exhibiting higher acne severity and insulin resistance levels.
5. The relationship between acne severity and insulin resistance was evident, with higher HOMA-IR levels observed in patients with severe acne compared to those with mild or moderate acne.

6. Conflict of Interest

Not available

7. Financial Support

Not available

8. References

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