Effect of Systemic Isotretinoin on serum Irisin level in Acne Vulgaris patients

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Abstract

Background: Acne vulgaris (AV) is a chronic inflammatory dermatological disorder affecting pilosebaceous unit. Clinically, it manifested as comedones, pustules, papules, nodules, cysts, and scarring on the face and trunk.

Objectives: Assess serum irisin levels in acne vulgaris, compare them with healthy controls, as well as analyze impact of oral isotretinoin on serum irisin in cases with AV.

Patients and methods: A prospective randomized clinical interventional trial was enrolled patients diagnosed clinically with moderate and severe acne vulgaris 40 AV patients were split into two groups based on Global Evaluation Acne Scale : group 1 was moderate AV, group 2 was severe AV. Serum irisin was measured in AV patients before and after oral isotretinoin treatment and compared to the control group (group 3).

Results: There was significant difference among three groups in median level of serum irisin before treatment (p = 0.002) i.e., median level was significantly lower in control group (32 [23 - 188] ng/ml) compared with both groups (moderate AV (38 (16-163) ng/ml) (p = 0.004) , severe AV (46 (25.5-113) ng/ml) (p = 0.008). After treatment, there was significant difference among three groups in median level of serum irisin (p = 0.017). There was a non-statistically significant difference among 2 groups regarding clinical improvement (p = 0.308), cases satisfaction (p = 0.527) and treatment side effects (p = 0.507).

Conclusion: Serum irisin serves as a biomarker for disease etiology and a potential prognostic indicator for severity of AV.

Keywords: Acne vulgaris; Serum irisin; Systemic isotretinoin.

DOI: 10.21608/SVUIJM.2025.392359.2192

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Received: 1June,2025.

Revised: 29 June, 2025.

Accepted: 30 June, 2025.

Published: 8 August, 2025

Cite this article as Soheir Abdel-Hamid, Nahed Mohamed Abou Elwfa, Essra Abass Abd Allah, Hassan M. Ibrahim. Effect of Systemic Isotretinoin on serum Irisin level in Acne Vulgaris patients. SVU-International Journal of Medical Sciences. Vol.8, Issue 2, pp: 332-348.

Introduction

AV was a persistent inflammatory dermatological condition impacting the pilosebaceous unit. Illness severity varies from mild comedonal acne to severe nodulocystic acne, which may result in permanent disfigurement. In addition to physical damage, AV can have a major impact on mental health, resulting in anxiety, despair, and low self-esteem **(Zaenglein et al., 2016).**

Pathophysiology was due to increased sebum production brought on by androgen, altered keratinization and infundibular epithelial inflammation, and Propionibacterium acnes colonization of hair follicles **(Toyoda and Morohashi, 2001).**

Adipokines may contribute to the etiology of AV, correlated with the severity of the condition. Irisin, a hormone-like myokine, was an adipokine exhibiting anti-inflammatory and antioxidant properties.**(Mustafa and El-Shimi, 2018)**.

Various therapies for AV exist, including retinoids, benzoyl peroxide, azelaic acid, and topical antibiotics. Systemic therapies such as isotretinoin, hormone therapy, and antibiotics. There was little evidence to support alternative therapies, including tea tree oil, low-glycemic-load meals, and pure bee venom, in addition to physical methods, including chemical peels, laser therapy, and light therapy. **(Ogé et al., 2019).**

Isotretinoin (13-cis retinoic acid) was the most effective known suppressor of sebum production. Isotretinoin works in a number of ways, including reducing Propionibacterium acnes proliferation, inhibiting inflammation, controlling keratinization patterns inside sebaceous gland follicles, and suppressing sebaceous gland activity. (**Ganceviciene and Zouboulis, 2010**).The aim of our research is to evaluate serum irisin levels in acne vulgaris and compare them with healthy controls and evaluate the effect of systemic isotretinoin on serum irisin in acne vulgaris patients.

Patients and methods

Study design and participants

This prospective randomized clinical trial (RCT) was carried out at the South Valley University Department of Dermatology, Venereology, and Andrology, Qena University Hospital, and Outpatient Clinic between March 2023 and November 2024. Healthy individuals experiencing moderate to severe AV, aged fourteen, older, who have not had any treatment for AV for a minimum length of six months. AV cases were excluded due to pregnancy and lactation, a history of osteoporosis or poor bone mineral density, intestinal problems including ulcerative colitis or inflammatory bowel disease, diabetes mellitus, depression or mental illness, hyperlipidemia, cardiovascular disease, renal disease, or chronic liver disease.

At least two months and two weeks before the research, respectively, no systemic or local acne medications had been utilized by any of the individuals. The control group included healthy individuals with age and sex, BMI matching, no history of acne, or other inflammatory or autoimmune disorders. In addition to a thorough history taking, each patient had a general and dermatological examination. In order to reach eighty percent power and a five percent level of significance (type 1 error), we modified the sample size (**Fig. 1).**

Randomization and masking

At random, patients were split into three groups (1:1:1): group 1 had moderate AV, group 2 had severe AV, and group 3 was the control. The process of randomization was carried out with closed envelopes. In contrast to patients and data interpreters, researchers and medical staff weren't blinded to the trial medication assignment.

Sample size calculation

We applied the G*power 3 algorithm (**Faul et al., 2007**) to determine the sample size. To examine the impact of oral isotretinoin on AV patients after three months with a measurement of serum irisin in AV patients compared with the control group, a sample size of at least 60 participants was predicted to be necessary, with an 80% power and a 0.05 error probability. For each participant, one of the three collections was assigned. This led to the creation of three

groups in the study: 20 patients with moderate AV, 20 patients with severe AV, both of whom received oral isotretinoin, and 20 healthy people as a control group.

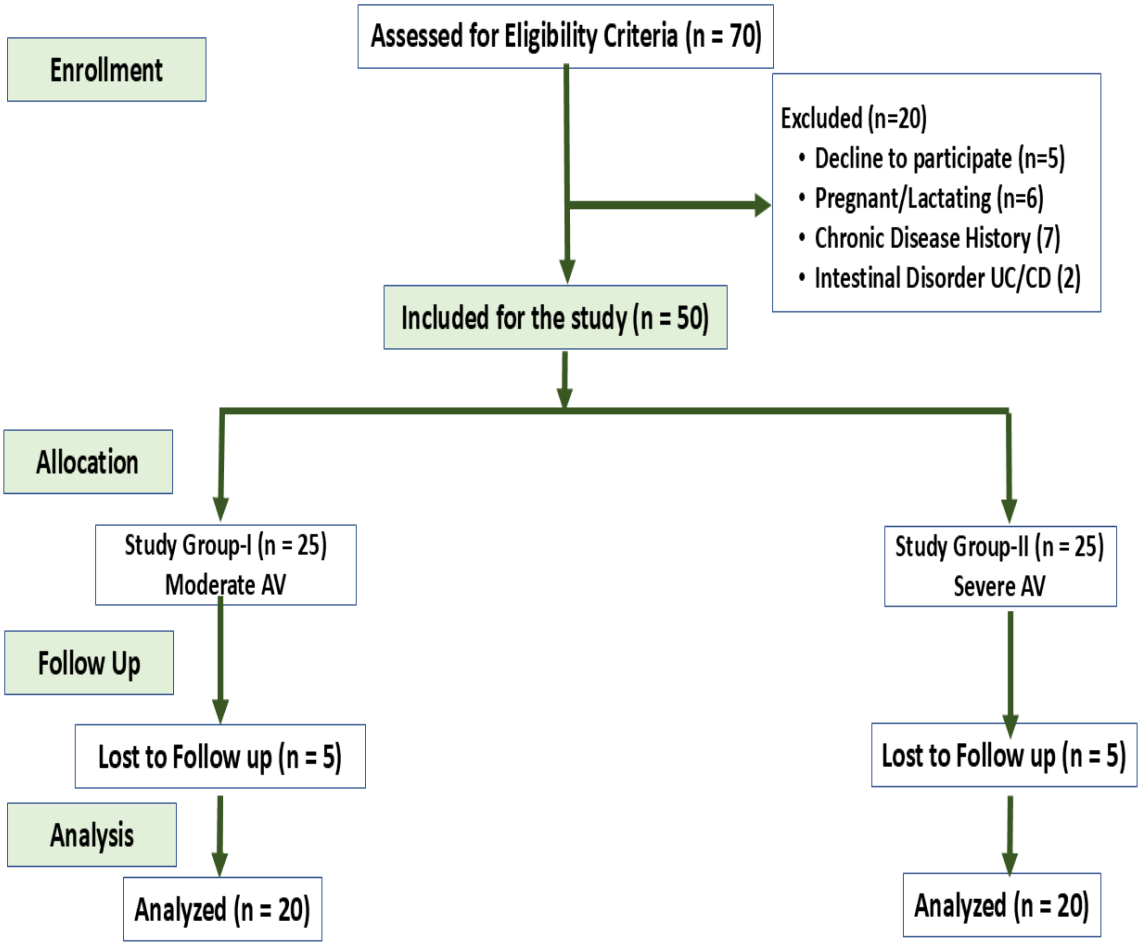

Fig.1. Consort flow diagram

Ethical considerations

The ethics committees of the South Valley University Faculty of Medicine approved the current study, which was given approval number SVU, MED, DVA021-1-23-3-605. The Institutional Review Board-Ethics Committee of South Valley University's Faculty of Medicine gave its approval to the study, which was conducted in accordance with the Declaration of Helsinki's principles.The study was registered on the clinical trial website as Identifier: NCT05869188 (https://clinicaltrials.gov/).

Additionally, a signed consent form was given to each participant. The goal of the study and their ability to join or withdraw at any moment without any obligations were made explicit in the informed consent. Additionally, each participant was given a code number that was used exclusively for analysis, guaranteeing their privacy and confidentiality. There were no incentives or prizes for the participants.

History and clinical examination

Comprehensive medical history that includes details on age, sex, work, residence, marital status, and unique habits and details about the disease, including its onset, course, duration, progression, and past history of AV; site of lesions; prior treatment history; and family history of AV or another autoimmune disorder. Complete clinical assessment, general and detailed dermatological assessment with particular

attention to the skin (characteristic AV lesions), hair, nails, and oral mucosa, and calculating BMI. Before starting treatment, AV patients who had not received any systemic or local acne treatments at least two weeks and two months before the study, respectively, followed the protocol for treatment.

Classification of patient

Based on the degree of acne severity, patients with acne vulgaris were divided into moderate and severe cases (**Global Evaluation Acne Scale: Dréno et al., 2011).**

The patients were divided into two groups (each group 20 cases) and a control group (20):

· Group 1: individuals with moderate cases of acne vulgaris.

· Group 2: individuals with severe cases of acne vulgaris.

· Group 3: control group.

Global Evaluation Acne Scale: (Dréno et al.2011)

- **0 - Clear. No lesions:** remaining pigmentation and erythema may be seen.
- **Almost clear. Almost no lesions:** A few occasional open or closed comedones and very few papules.
- **Mild Easily recognizable:** Less than half of the face was affected. A few open or closed comedones, together with a few papules and pustules.
- **Moderate:** Over half of the face was affected. Many papules and pustules, as well as many open or closed comedones. One nodule may be present.
- **Severe:**There were open or closed comedones, sporadic nodules, and a large number of papules and pustules throughout the entire face.
- **Very Severe:** Acne on the face that is extremely inflammatory and has nodules.

Quantitative assay of serum irisin level

Before starting systemic retinoid treatment and then after three months of treatment. Two milliliters of whole blood were obtained from the anterior cubital fossa of all participants, including the control group. The region is disinfected with seventy percent methylated alcohol/spirit and permittedto dry completely prior to blood collection. Blood was promptly placed in a red-capped Vacutainer. The specimen vial was gently mixed to prevent hemolysis. Blood samples were thereafter conveyed to the laboratory within two hours of collection. Samples were centrifuged in the laboratory to extract serum. Serum samples were thereafter aliquoted and preserved at −86° Celsius until a certain quantity of samples were collected for batch testing. The Human Irisin ELISA Kit CATALOG #:95512 (Glory Science Co., Ltd.; Taiwan; China) is an enzyme-linked immunosorbent assay used to determine the level of serum irisin using an ELISA reader (EMR-500, USA).

Dermatological evaluation of the patients included

Clinical evaluations: Standardized high-resolution digital images utilizing consistent camera settings (Xiaomi Redmi) (China) were obtained at baseline, during treatment, and after treatment. Evaluation of clinical improvement based on both lesion count changes and IGA scale success yields both quantitative and qualitative assessments of acne, providing helpful supplementary data. Clinical improvement is evaluated using the following criteria: G4 (excellent: 100% reduction), G3 (good: 75-99% reduction), G2 (moderate: 50-74% reduction), G1 (insufficient: 1-49% reduction), G0 (unchanged), and G-1 (worse).(Witkowski J and Parish LC, 2004)

Clinical Satisfaction: A three-point evaluation system was used to record patient satisfaction, with grade 3 representing "highly satisfied," grade 2 representing "satisfied," and grade 1 representing "dissatisfied."

•Follow up the laboratory investigations after one month of treatment and then after treatment.

•Assessment of side effects of systemic isotretinoin.

Statistical analysis

The researcher used SPSS version 24* for data analysis, verification, and coding.

Descriptive statistics: Standard deviations (SD), averages, and percentages were calculated. Tests of significance: The chi-square test was used to compare the differences in frequency distributions among multiple groups. The ANOVA/Kruskal-Wallis test was used to assess the mean/median differences of the data (parametric and non-parametric, respectively), and the post-hoc test was calculated using Bonferroni corrections for continuous variables with more than two categories. For repeated measures (pre- vs. post-treatment), the paired sample t-test was utilized. The student t-test was used to examine the mean differences in continuous variables between groups. Pearson's correlation was calculated to investigate the association between s. irisin and disease markers. A significant p-value was defined as 0.05 or less.

Results

In the current study, forty patients with moderate (n = 20) and severe (n = 20) acne vulgaris were chosen from the Dermatology, Venereology, and Andrology Department outpatient clinic at Qena University hospitals. Twenty healthy people formed the control group.

Regarding baseline characteristic, control group was significantly (p = 0.003) older compared with both treatment groups. The three groups were matched for sex (p = 0.057). Married represented significantly (p = 0.001) higher percentage (60%) in the control group compared with the moderate and severe AV groups. Further, there was insignificant difference (p = 0.549 and 0.059) in the distribution of sample regarding residence and occupation. Likely, there was insignificant difference (p = 0.067) in distribution of sample respecting special habits. As well, the mean BMI was insignificantly (p = 0.202) different between the studied groups, (**Table.1).**

Table 1. Baseline Characteristic Differences among Studied Groups

Variables	Control (n = 20)	Moderate AV (n = 20)	Severe AV (n = 20)	P-value
Age/year	24.2 ± 5.1	21.10 ± 5.6	22.05 ± 5.4	**= 0.003***
P-value**	**I vs. II = 0.001**	II vs. III = 0.584	**I vs. III =0.007**	
Sex				= 0.057***
• **Women**	9 (45%)	14 (70%)	16 (80%)	
• **Male**	11 (55%)	6 (30%)	4 (20%)	
Marital Status				
• **Single**	8 (40%)	17 (85%)	18 (90%)	**= 0.001*****
• **Married**	12 (60%)	3 (15%)	2 (10%)	
Residence				
• **Rural**	11 (55%)	11 (55%)	8 (40%)	= 0.549***
• **Urban**	9 (45%)	9 (45%)	12 (60%)	
Occupation				
• **Housewife**	5 (25%)	3 (15%)	1 (5%)	
• **Student**	7 (35%)	15 (75%)	16 (80%)	= 0.059***
• **Employed**	8 (40%)	2 (10%)	3 (15%)	
Special Habits				
• **Non-smoker**	14 (70%)	19 (95%)	18 (90%)	= 0.067***
• **Smoker**	6 (30%)	1 (5%)	2 (10%)	

BMI	28.22 ± 5.1	26.53 ± 2.7	26.19 ± 3.3	= 0.202*
• **P-value****	I vs. II = 0.165	II vs. III = 0.775	I vs. III =0.096	

*ANOVA test was used to compare the mean difference between groups; **Post-hoc test was used for pairwise comparison with Bonferroni correction; ***Chi-square test was used to compare the proportion difference between groups

There was no statistically significant difference among the 2 groups regarding family history (p = 0.744), disease duration (p = 0.492), history of previous treatment (p = 0.723), past history (p = 0.490), or lesion site (p = 1.000).(**Table. 2).**

Table 2.Clinical Data Differences among Studied Groups

Variables	Moderate AV (n = 20)	Severe AV (n = 20)	P-value
Family History			
• **Negative**	12 (60%)	13 (65%)	= 0.744*
• **Positive**	8 (40%)	7 (35%)	
Disease Duration/year	2.01 ± 0.9	1.83 ± 0.7	= 0.492**
Previous Treatment			
• **No**	6 (30%)	5 (25%)	= 0.723*
• **Yes**	14 (70%)	15 (75%)	
Past-history			
• **Primary**	7 (35%)	5 (25%)	= 0.490*
• **Recurrent**	13 (65%)	15 (75%)	
Lesion Site (Face)	20 (100%)	20 (100%)	= 1.000*

*Chi-square test was used to compare the proportion difference between groups; **Independent Sample t-test was used to compare the mean difference between groups.

There was no statistically significant difference among the 2 groups regarding clinical improvement (p = 0.308), patients' satisfaction (p = 0.527), and treatment side effects (p = 0.507).(**Table.3)**

Table 3. Outcome Findings among Studied Groups

Variables	Moderate AV (n = 20)	Severe AV (n = 20)	P-value
Clinical Improvement			= 0.308*
• **Insufficient**	3 (15%)	4 (20%)	
• **Moderate**	13 (65%)	8 (40%)	
• **Good**	4 (20%)	8 (40%)	
Patients' Satisfaction			
• **Unsatisfied**	11 (55%)	9 (45%)	= 0.527*
• **Satisfied**	9 (45%)	11 (55%)	
Side Effects			
• **No**	6 (30%)	8 (40%)	= 0.507*
• **Yes**	14 (70%)	12 (60%)	

*Chi-square test was used to compare the proportion difference between groups

(Fig.2). showed a female patient with moderate AV (a) prior to isotretinoin and (b) after receiving isotretinoin showed good clinical improvement. (**Fig. 3**) A female patient with severe AV (a) prior to isotretinoin and (b) after receiving isotretinoin showed good clinical improvement.

Fig.2: A female patient with moderate AV (a) prior to isotretinoin and (b) after receiving isotretinoin showed good clinical improvement.

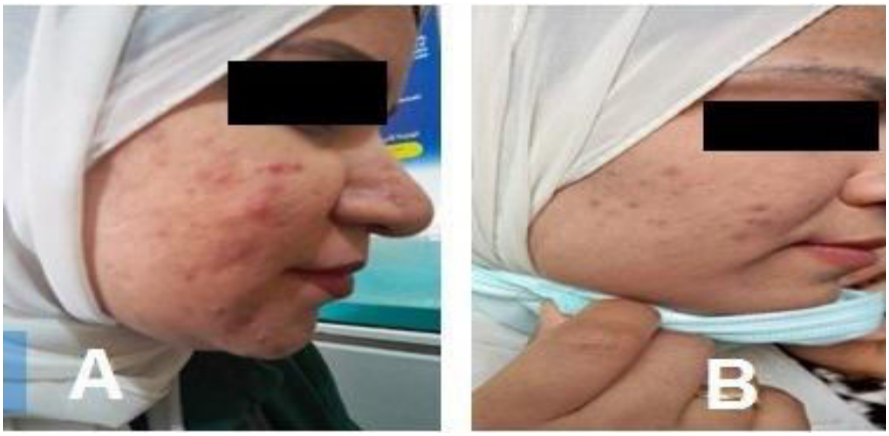

Fig.3: A female patient with severe AV (a) prior to isotretinoin and (b) after receiving isotretinoin showed good clinical improvement.

Effect of treatment on S. irisin level among groups. There was a significant difference among 3 groups in median level of serum irisin before treatment (p = 0.002); i.e., the median level was significantly lower in the control group (32 [23 - 188] ng/ml) compared with both case groups (moderate AV (38 [16 - 163] ng/ml) (p = 0.004) and severe AV (46 [25.5 - 113] ng/ml) (p = 0.008)). After treatment, there was a significant difference among 3 groups in median level of serum irisin (p = 0.017).(**Table.4).**

Table 4. Difference in S. Irisin Level between Studied Groups

Variables	Control (n = 20)	Moderate AV (n = 20)	Severe AV (n = 20)	P-value
S. Irisin (ng/ml) Before Treatment				
• **Mean ± SD**	39.56 ± 35.4	54.23 ± 32.1	50.84 ± 22.3	
• **Median (Range)**	32 (23-188)	38 (16-163)	46 (25.5-113)	**= 0.002***
P-value**	**I vs. II = 0.004**	II vs. III = 0.897	**I vs. III =0.008**	
S. Irisin (ng/ml) After Treatment				
• **Mean ± SD**	39.56 ± 35.4	24.64 ± 9.3	38.33 ± 33.9	
• **Median (Range)**	32 (23-188)	21 (10-44)	25.5 (11-160)	**= 0.017***
P-value**	**I vs. II =**	II vs. III = 0.059	I vs. III =0.889	

	0.013			
P-value* **	= 1.000	**= 0.001**	**< 0.001**	

*Kruskal Wallis test was used to compare the mean difference between groups; **Post-hoc test was used for pairwise comparison with Bonferroni correction; ***Paired Sample t-test was used to compare the difference in mean within group

Effect of treatment on laboratory findings among cases.Regarding serum AST, moderate AV had significantly (p=0.003) increased mean level of s. AST before treatment compared with those with severe AV. Likely, after treatment, there was significant difference among cases in mean level of serum AST (p<0.001). For within group comparisons, there was significant (p<0.001) reduction in both groups. Respecting serum ALT, cases with moderate AV had significantly (p<0.001) increase mean level before treatment compared with those with severe AV. Likely, after treatment, there was significant difference among the cases in mean level of serum ALT (p<0.001). For within group comparisons, there was significant (p<0.001) reduction in both groups.

For the serum creatinine and serum cholesterol, there was no significant difference in mean level either before or after treatment. For within-group comparisons, there was an insignificant reduction in both groups.

Furthermore, cases with severe AV had significantly (p<0.001) higher mean levels of serum TGD before treatment compared with those with moderate AV. Also, after treatment, there was a significant difference between the cases in the mean level of serum TGD (p<0.001). For within-group comparisons, the moderate AV group showed a significant (p<0.001) high in the mean level, while there was a significant (p<0.001) reduction in the mean level for cases with severe AV. (**Table.5).**

Table 5. Difference in Laboratory Findings among Studied Groups

Variables	**Moderate AV (n = 20)**	**Severe AV (n = 20)**	**P-value**
S. AST (U/L)			
• **Before treatment**	27.90 ± 4.1	23.95 ± 3.6	**= 0.003***
• **After treatment**	25.01 ± 3.9	20.30 ± 3.7	**< 0.001***
P-value**	**< 0.001**	**< 0.001**	
S. ALT (U/L)			
• **Before treatment**	30.10 ± 3.8	24.95 ± 4.2	**< 0.001***
• **After treatment**	25.75 ± 3.1	21.55 ± 5.2	**= 0.004***
P-value**	**< 0.001**	**< 0.001**	
S.Creatinine (mg/dl)			
• **Before treatment**	0.29 ± 0.1	0.32 ± 0.1	= 0.392*
• **After treatment**	0.25 ± 0.1	0.26 ± 0.1	= 0.979*
P-value**	= 0.339	= 0.401	
S.Cholesterol (mg/dl)			
• **Before treatment**	77.05 ± 14.1	81.70 ± 13.3	= 0.288*
• **After treatment**	79.75 ± 14.9	78.90 ± 11.6	= 0.841*
P-value**	= 0.143	= 0.141	
S. TGD (mg/dl)			
• **Before treatment**	56.15 ± 12.1	97.45 ± 12.2	**< 0.001***
• **After treatment**	60.75 ± 12.7	91.05 ± 10.8	**< 0.001***
P-value**	**< 0.001**	**< 0.001**	

*Independent Sample t-test was used to compare the mean difference between groups; **Paired Sample t-test was used to compare the difference in mean within group

Correlation among serum irisin level before and after treatment and disease determinants (**Table.6).** For the total sample, there was a significant negative moderate correlation between S. irisin before treatment and disease duration (r = -0.295, p = 0.032). There was a significant positive moderate correlation between S. irisin after treatment and age (r = 0.238, p = 0.048). (**Fig. 4**). For the **moderate AV group**, there was a significant negative moderate correlation between S. irisin before treatment and disease duration (r = -0.505, p = 0.012). Likewise, males had significantly lower levels of S. irisin after treatment than females (r = -0.454, p = 0.022); there was a significant positive moderate correlation among S. irisin after treatment and cases of MBI (r = -0.428, p = 0.030). (**Fig. 5**). For the **severe AV group**, males had significantly lower levels of S. irisin after treatment than females (r = -0.401, p = 0.040). Likely, there was a significant negative moderate correlation between S. irisin after treatment and disease duration (r = -0.442, p = 0.025). (**Fig. 6**).

Table 6. Correlation between S. Irisin and Disease Determinants

Variables	S. Irisin Before treatment	S. Irisin After treatment
	r* (P-value**)	
Total Sample		
• **Age**	0.048 (p = 0.369)	**0.238 (p = 0.048)**
• **Sex**	-0.092 (p = 0.262)	-0.208 (p = 0.074)
• **BMI**	0.065 (p = 0.326)	-0.213 (p = 0.069)
• **Disease Duration**	**-0.295 (p = 0.032)**	-0.255 (p = 0.081)
• **Past-history**	0.097 (p = 0.276)	0.137 (p = 0.199)
• **Family History**	-0.166 (p = 0.154)	-0.150 (p = 0.128)
• **Treatment History**	-0.136 (p = 0.202)	-0.163 (p = 0.158)
• **Clinical Improvement**	-0.133 (p = 0.207)	0.243 (p = 0.065)
• **Patients' Satisfaction**	-0.052 (p = 0.375)	0.262 (p = 0.051)
• **Side Effects**	0.141 (p = 0.193)	-0.216 (p = 0.091)
Moderate AV Group		
• **Age**	0.347 (p = 0.067)	0.319 (p = 0.085)
• **Sex**	-0.114 (p = 0.317)	**-0.454 (p = 0.022)**
• **BMI**	0.272 (p = 0.123)	**-0.428 (p = 0.030)**
• **Disease Duration**	**-0.505 (p = 0.012)**	-0.012 (p = 0.497)
• **Past-history**	0.245 (p = 0.148)	0.155 (p = 0.258)
• **Family History**	-0.035 (p = 0.441)	-0.001 (p = 0.499)
• **Treatment History**	-0.322 (p = 0.083)	-0.151 (p = 0.262)
• **Clinical Improvement**	-0.255 (p = 0.170)	-0.257 (p = 0.137)
• **Patients' Satisfaction**	0.200 (p = 0.198)	0.253 (p = 0.141)
• **Side Effects**	0.038 (p = 0.437)	-0.227 (p = 0.165)
Severe AV Group		
• **Age**	-0.206 (p = 0.192)	-0.061 (p = 0.397)
• **Sex**	-0.098 (p = 0.341)	**-0.401 (p = 0.040)**
• **BMI**	0.136 (p = 0.289)	-0.019 (p = 0.486)
• **Disease Duration**	-0.109 (p = 0.323)	**-0.442 (p = 0.025)**
• **Past-history**	-0.010 (p = 0.483)	-0.210 (p = 0.187)
• **Family History**	-0.236 (p = 0.158)	-0.264 (p = 0.131)

• **Treatment History**	0.010 (p = 0.483)	-0.210 (p = 0.187)
• **Clinical Improvement**	0.050 (p = 0.417)	0.171 (p = 0.235)
• **Patients' Satisfaction**	0.296 (p = 0.102)	0.227 (p = 0.168)
• **Side Effects**	0.217 (p = 0.184)	-0.204 (p = 0.195)

*Pearson's correlation coefficient; **Based on normal approximation

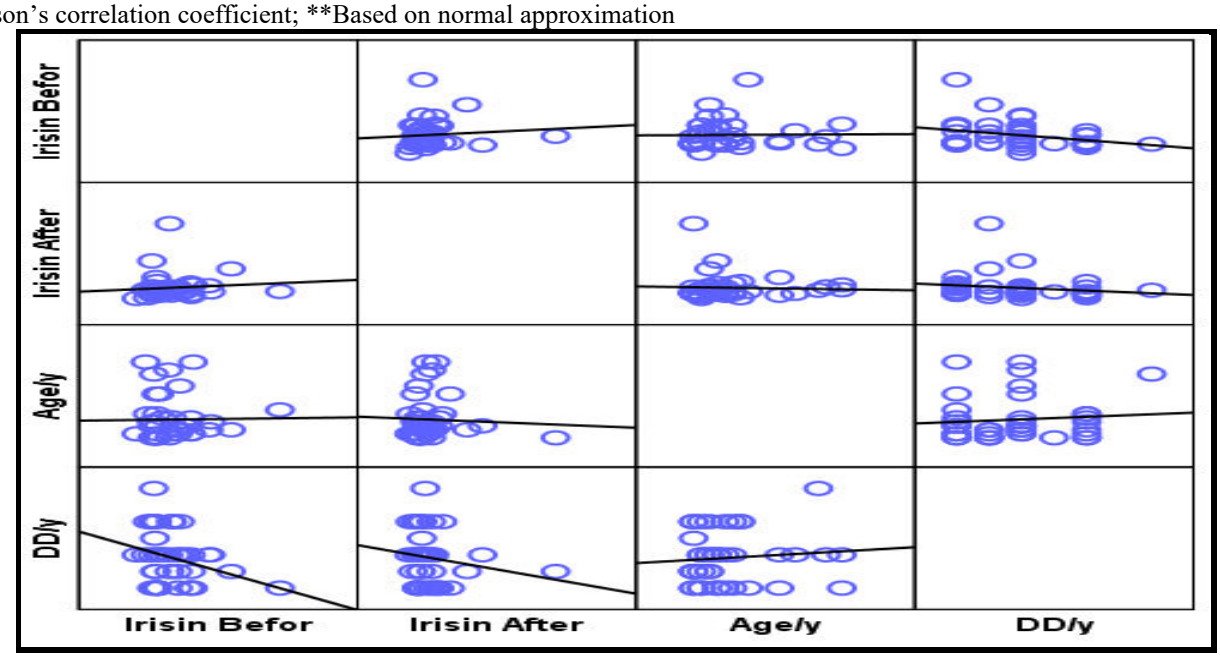

Fig. 4. Correlation of S. Irisin and Disease Determinants (Total Sample)

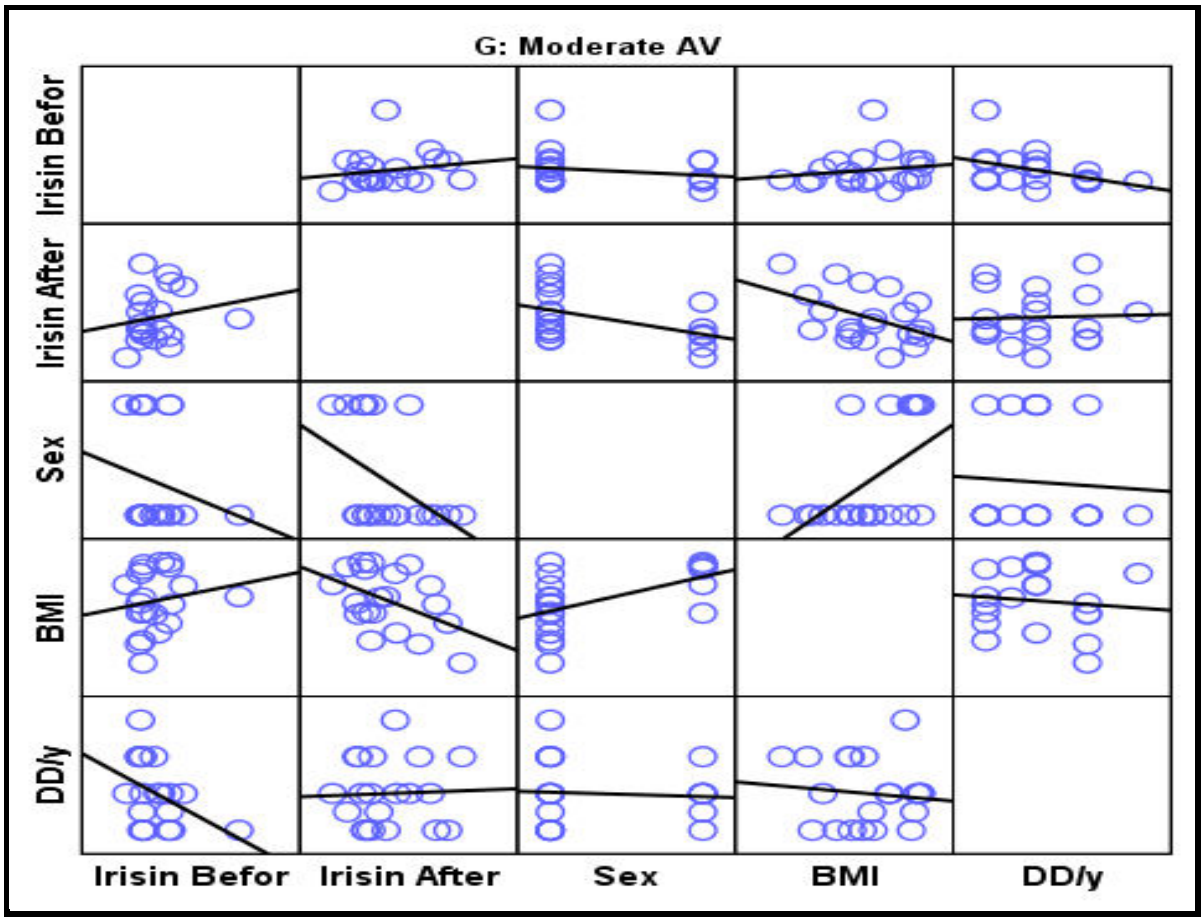

Fig. 5. Correlation of S. Irisin and Disease Determinants (Moderate Group)

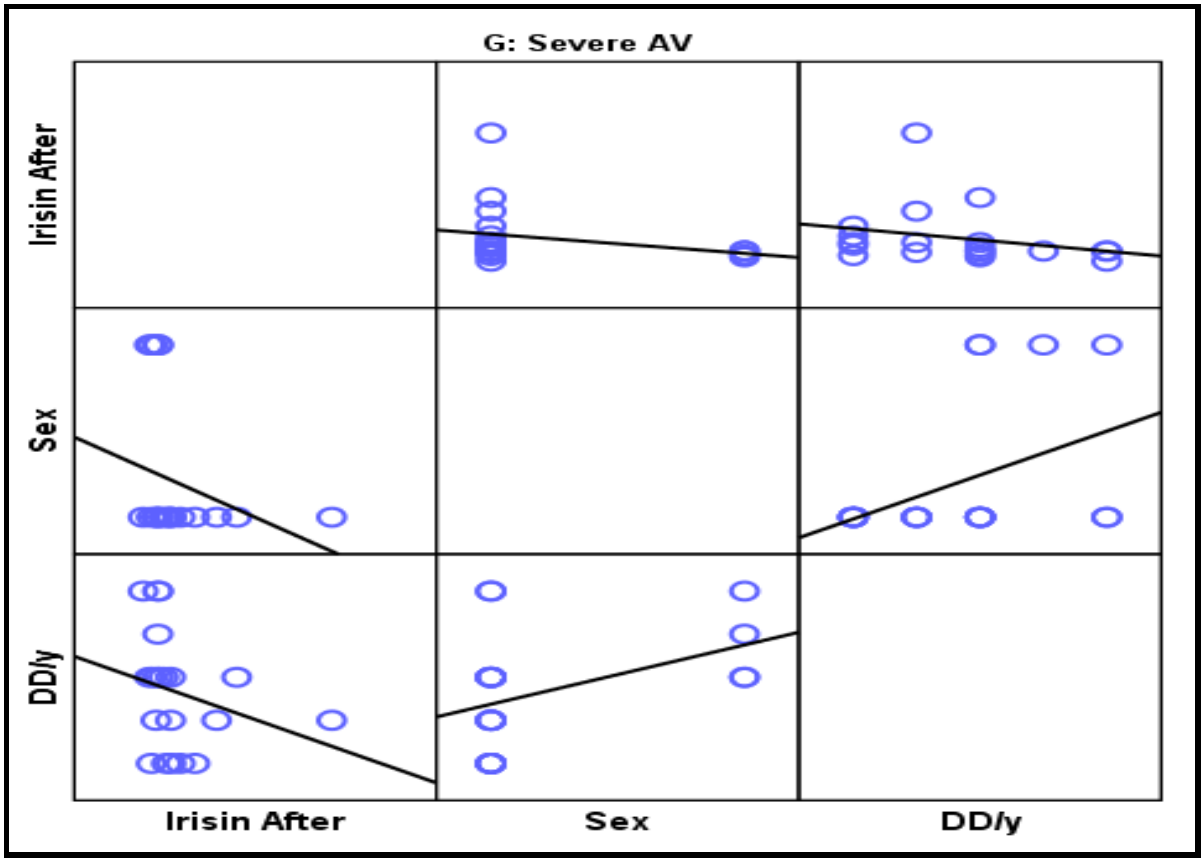

Fig. 6. Correlation of S. Irisin and Disease Determinants (Severe Group)

Multivariable logistic regression model of predictors of AV disease. For the total sample, there were four predictors (age, serum irisin before treatment, sex, and serum irisin after treatment) after adjusting for all variables. With a one-year increase in age, there was a 20% low in liability for AV. Men's cases were ninety-one percent (OR = 0.093, ninety-five percent CI; 0.015 – 0.564, p = 0.010) less liable for AV than females. With one ng/dl high in level of serum irisin before treatment, there was four percent (OR = 1.041, ninety-five percent CI; 1.003 – 1.080, p = 0.036) high in risk of AV. As well, with one ng/dl high in level of serum irisin after treatment, there was a four percent (OR=0.961, ninety-five percent CI; 0.931–0.992, p = 0.015) reduction in AV probability. For moderate AV prediction, there were four predictors (age, sex, s.irisin before treatment, and s.irisin after treatment) after adjusting for all variables. In other words, with a one-year increase in age, there was a nine percent (OR = 0.809, ninety-five percent CI; 0.657 – 0.995, p = 0.045) decrease in liability for AV. Male cases were ninety-two percent (OR = 0.882, ninety-five percent CI; 0.008 – 0.890, p = 0.040) less liable for AV than females. With one ng/dl low in level of S. irisin before treatment, there was thirty-three percent (OR = 1.329, ninety-five percent CI; 0.989 – 1.000, p = 0.050) high risk of AV. As well, with one ng/dl high in level of s. irisin after treatment, there was a twenty-six percent (OR=0.740, ninety-five percent CI; 0.562–0.974, p = 0.032) reduction in AV probability. For severe AV prediction, it was found that sex was the only predictor after adjusting for all variables; i.e., male patients were 89% (OR=0.114, 95% CI; 0.014–0.752, p = 0.024) less liable for AV than females.(**Table.7).**

Table 7: Independent Predictors of AV: Multivariable Logistic Regression Model

Variables	OR (95% CI) *	P-value
Total Sample		
• **Age**	0.803 (0.690 – 0.933)	**= 0.004**
• **Sex (Male)**	0.093 (0.015 – 0.564)	**= 0.010**
• **BMI**	0.922 (0.770 – 1.103)	= 0.372
• **S. Irisin Before treatment**	1.041 (1.003 – 1.080)	**= 0.036**
• **S. Irisin After treatment**	0.961 (0.931 – 0.992)	**= 0.015**
Moderate AV		
• **Age**	0.809 (0.657 – 0.995)	**= 0.045**
• **Sex**	0.082 (0.008 – 0.890)	**= 0.040**
• **BMI**	0.953 (0.760 – 1.197)	= 0.681
• **S. Irisin Before treatment**	1.392 (0.989 – 1.000)	**= 0.050**
• **S. Irisin After treatment**	0.740 (0.562 – 0.974)	**= 0.032**
Severe AV		
• **Age**	0.882 (0.747 – 1.042)	= 0.140
• **Sex**	0.114 (0.017 – 0.752)	**= 0.024**
• **BMI**	0.947 (0.723 – 1.240)	= 0.691
• **S. Irisin Before treatment**	1.023 (0.981 – 1.1067)	= 0.281
• **S. Irisin After treatment**	0.972 (0.946 – 1.010)	= 0.171

OR=Odds Ratio; CI, Confidence Interval

Discussion

AV is a persistent, complicated inflammatory condition affecting the pilosebaceous units of the skin. AV affects over the long term and is characterized by chronic inflammation, hyperkeratinization, and desquamation. (**Thiboutot et al., 2018).** Numerous host factors, including cellular immunological responses, dysbiosis of the pilosebaceous follicle microbiome, and circulating androgens that activate sebaceous glands, interact to cause acne vulgaris. Numerous factors, including diet and genetics, may have an impact on the onset and course of the illness. The primary lesion and precursor of all clinical manifestations of acne vulgaris was the microcomedo. **(Hall et al., 2018).**

Irisin is a recently identified myokine with adipokine properties that is released into the bloodstream in response to physical exercise. While the cytoplasm contains the C-terminal tail of FNDC5, the extracellular N-terminal portion was cleaved and released as irisin. **(Boström et al., 2012; Chen et al., 2016).**

Topical antibiotics, benzoyl peroxide, azelaic acid, and retinoids are some of the therapy options for acne vulgaris. Systemic therapies such isotretinoin, hormone therapy, and antibiotics **(Oge et al., 2019).** Isotretinoin, as a systemic retinoid and a metabolite of vitamin A (retinol), is the only medication that may be used to treat acne by affecting the pilosebaceous units of the skin. AV affects pathogenic pathways linked to the disorder. Despite being a successful and generally well-tolerated medication, isotretinoin consumption was linked to a number of side effects. **(Hermans and Valensi, 2018; Katsambas and Papakonstantinou, 2004).** Furthermore, isotretinoin reduces acne by causing sebaceous glands to undergo apoptosis, which shrinks the glands **(Nelson et al., 2008).**

Our findings align with those of **Strauss et al. (2007**), who indicated that isotretinoin was used for the treatment of severe acne that was resistant to other therapies or that led to physical or psychological scarring. Standard dosage ranges from 0.5 to 2.0 mg/kg/day, typically administered over a twenty-four-week period. **Ahmad (2015**) conducted a study involving fifty-eight cases of acne vulgaris, who were randomized into two groups: group I received a once-daily dose, while group II received a twice-daily dose of oral isotretinoin. Results indicated that both

regimens led to a highly significant clinical improvement in acne.

Baseline socio-demographic characteristics of studied groups. The control group was significantly (p = 0.003) older compared with both treatment groups. The three groups were matched for sex (p = 0.057). Married represented a significantly (p = 0.001) higher percentage (60%) in the control group compared with the moderate and severe AV groups. Further, there was an insignificant difference (p = 0.549 and 0.059) in the distribution of the sample regarding residence and occupation. Likely, there was an insignificant difference (p = 0.067) in the distribution of the sample respecting special habits. As well, the mean BMI was insignificantly (p = 0.202) different between the studied groups.

According to the end findings of analyzed cases, our results indicated no statistically significant difference between the two groups in terms of treatment side effects (p = 0.507). In terms of side effects, fourteen (seventy percent) cases in the moderate AV group and twelve (sixty percent) cases in the severe AV group experienced adverse effects. Such were dryness of lips, face, and eyes, as well as menstruation irregularity. In accordance with **Garba et al. (2020**), acne cases undergoing treatment with 13-cis-retinoic acid within a cohort of 230 individuals. Their investigation indicated that predominant side effects observed were dry, chapped lips in one hundred eight (forty percent) of cases, dry skin in seventy-eight (forty percent), nosebleeds in eleven percent, and weariness in five percent.

Regarding end findings of analyzed cases, our results indicated no statistically significant difference among two groups in terms of clinical improvement (p = 0.308). Concerning clinical improvement, in the moderate AV group, 3 (fifteen percent) patients exhibited insufficient improvement, 13 (sixty-five percent) showed moderate improvement, and 4 (twenty percent) showed considerable improvement. In the severe AV group, clinical improvement was inadequate in four (twenty percent) patients, moderate in eight (forty percent) cases, and substantial in eight (forty percent) cases. In a study by **Newton et al. (1997)**, it was demonstrated that case-assessed outcome measures can reflect temporal changes and differentiate among treatments with varying effectiveness. Findings indicated a statistically significant improvement in clinical outcomes at 4 months in the majority of cases-assessed measures at 1 year compared to baseline.

According to the end findings of analyzed cases, our results indicated no statistically significant difference between the two groups in terms of case satisfaction (p=0.507).In contrast to the research conducted by **Bhushan et al. (2024**), which sought to evaluate the impact of isotretinoin on quality of life (QoL) in cases with acne vulgaris over a six-month follow-up period, It was shown that quality of life considerably improves among cases with acne vulgaris following oral isotretinoin medication.

Our findings indicated that treatment's influence on serum irisin was observed. There was a significant difference among 3 groups in median level of serum irisin before treatment (p = 0.002); i.e., the median level was significantly lower in the control group (32 [23 - 188] ng/ml) compared with both case groups (moderate AV (38 [16 - 163] ng/ml) (p = 0.004) and severe AV (46 [25.5 - 113] ng/ml) (p = 0.008)). After treatment, there was a significant difference among 3 groups in the median level of serum irisin (p = 0.017). Our results contrast those of **Ali et al. (2022**), who observed a statistically significant elevation in serum irisin levels in controls compared to cases with acne vulgaris (P < 0.001). Against those of **Mustafa and El-Shimi (2018**) who assessed serum irisin levels in individuals with acne vulgaris to examine its link with disease development. They established that serum irisin levels were considerably decreased in cases with acne vulgaris compared to the control group (P < 0.001).Against the findings of **Tang et al. (2022**), who examined the role of serum irisin as an adipokine to evaluate its function in the etiology of AV, the study comprised 171 participants: 115 cases with newly diagnosed

AV and 56 healthy individuals. Serum irisin levels in AV cases were recorded as (24.0 ± 11.3) ng/dl, compared to (104.3 ± 27.0) ng/dl in the control group, indicating a statistically significant reduction in AV cases ($P < 0.001$). Regarding the impact of therapy on laboratory results in our cases, moderate AV had a significantly ($p=0.003$) increased mean level of serum AST before treatment compared with those with severe AV. Likely, after treatment, there was a significant difference among cases in the mean level of serum AST ($p < 0.001$). For within-group comparisons, there was a significant ($p<0.001$) reduction in both groups. Respecting serum ALT, cases with moderate AV had a significantly ($p<0.001$) increased mean level before treatment compared with those with severe AV. Likely, after treatment, there was a significant difference among the cases in mean level of serum ALT ($p<0.001$). For within-group comparisons, there was a significant ($p<0.001$) reduction in both groups.

For the serum creatinine and serum cholesterol, there was no significant difference in mean level either before or after treatment. For within-group comparisons, there was an insignificant reduction in both groups. Furthermore, cases with severe AV had significantly ($p<0.001$) higher mean levels of serum TGD before treatment compared with those with moderate AV. Also, after treatment, there was a significant difference between the cases in the mean level of serum TGD ($p<0.001$). For within-group comparisons, the moderate AV group showed a significant ($p<0.001$) high in the mean level, while there was a significant ($p<0.001$) reduction in the mean level for cases with severe AV.

Findings were corroborated by **Ertugrul et al. (2011**), who indicated that, relative to baseline measurements, levels of AST, ALT, TC, LDL-C, and triglycerides were considerably elevated ($P < 0.01$, < 0.05, < 0.01, < 0.05, < 0.01, respectively). Our results aligned with those of **Soyuduru et al. (2019**), who established that in pre-treatment evaluation, there were no statistically significant variations in total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride levels among acne vulgaris cases and control groups. Comparing pre-treatment and post-treatment measures, isotretinoin treatment led to a statistically significant elevation in mean total cholesterol ($P < 0.001$), LDL cholesterol ($P = 0.002$), and triglycerides ($P = 0.009$). In contrast, there was a notable reduction in HDL cholesterol ($P = 0.0028$) after therapy.

In the current investigation concerning the link among serum irisin levels before and after therapy and illness determinants, for the total sample, there was a significant negative moderate correlation between S. irisin before and disease duration ($r = -0.295$, $p = 0.032$). There was a significant positive moderate correlation between S. irisin after treatment and case age ($r = 0.238$, $p = 0.048$). (Fig. 3). For the moderate AV group, there was a significant negative moderate correlation between S. irisin before treatment and disease duration ($r = -0.505$, $p = 0.012$). Likewise, males had significantly lower levels of S. irisin after treatment than females ($r = -0.454$, $p = 0.022$), and there was a significant positive moderate correlation among S. irisin after treatment and cases of MBI ($r = -0.428$, $p = 0.030$). (Fig. 4). For the severe AV group, males had significantly lower levels of S. irisin after treatment than females ($r = -0.401$, $p = 0.040$). Likely, there was a significant negative moderate correlation between S. irisin after treatment and disease duration ($r = -0.442$, $p = 0.025$).

Çalık et al. (2022) indicated that no correlation was seen among age, gender, and irisin levels. Recent research indicates that age and gender do not correlate with serum irisin levels. Unexpectedly, research indicates that serum irisin levels rise (**Li et al., 2017; Mehrabian et al., 2016; Lee et al., 2015**).

As regards the multivariable logistic regression model of predictors of AV disease. For the total sample, there were four predictors (age, serum irisin before treatment, sex, and serum irisin after treatment) after adjusting for all variables. With a one-year increase in age, there was a 20% (OR = 0.803, ninety-five percent CI; 0.690–0.933, p =

0.004) low in liability for AV. Men's cases were ninety-one percent (OR = 0.093, ninety-five percent CI; 0.015 – 0.564, p = 0.010) less liable for AV than females. With one ng/dl high in level of serum irisin before treatment, there was four percent (OR = 1.041, ninety-five percent CI; 1.003 – 1.080, p = 0.036) high in risk of AV. As well, with one ng/dl high in level of serum irisin after treatment, there was a four percent (OR=0.961, ninety-five percent CI; 0.931–0.992, p = 0.015) reduction in AV probability. For moderate AV prediction, there were four predictors (age, sex, s.irisin before treatment, and s.irisin after treatment) after adjusting for all variables. In other words, with a one-year increase in age, there was a nine percent (OR = 0.809, ninety-five percent CI; 0.657 – 0.995, p = 0.045) decrease in liability for AV. Male cases were ninety-two percent (OR = 0.882, ninety-five percent CI; 0.008 – 0.890, p = 0.040) less liable for AV than females. With one ng/dl low in level of S. irisin before treatment, there was thirty-three percent (OR = 1.329, ninety-five percent CI; 0.989 – 1.000, p = 0.050) high risk of AV. As well, with one ng/dl high in level of s. irisin after treatment, there was a twenty-six percent (OR=0.740, ninety-five percent CI; 0.562–0.974, p = 0.032) reduction in AV probability. For severe AV prediction, it was found that sex was the only predictor after adjusting for all variables; i.e., male patients were 89% (OR=0.114, 95% CI; 0.014–0.752, p = 0.024) less liable for AV than females.

This investigation corroborated findings of **Mustafa and El-Shimi (2018)**, which indicated that reduced serum irisin serves as both a biomarker for disease development and a potential prognostic indicator for severity of acne vulgaris. Our findings were corroborated by **Ali et al. (2022)**, who demonstrated that ROC curve analysis indicated a serum irisin threshold of less than or equal to 2.63 ng/ml was significant for identifying severe types of acne in cases, exhibiting optimal sensitivity and specificity (P = 0.001). Our results aligned with those of **Tang et al. (2022**); they reported a cutoff point of 53.32, a specificity of 92.8%, and an irisin sensitivity of 100.0%. According to their findings, serum irisin seems to be a promising predictive and diagnostic indicator. This relationship needed to be confirmed by more multi-center research, which could help with the creation of novel treatment alternatives.

Limitation: The study was limited by no follow-up to patients after treatment and a small sample size. Therefore, it might be required to carry out more extensive research in the future and follow up.

Conclusion

Acne vulgaris is a complex interplay of inflammatory diseases. Serum irisin serves as a marker for disease etiology.

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