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Investigation of the Effects of SOD1 +35A/C and GPx-3 +1494A/G Gene Polymorphisms in Patients With Acne Vulgaris

Fulya Yukcu,[1] Raziye Akcılar,[2] Nazlı Dizen Namdar,[3] Sevgi Kocyigit Sevinc,[1] Selve Arslan Utku[3]

[1]Department of Biophysics, Kutahya Health Sciences University Faculty of Medicine, Kutahya, Türkiye
[2]Department of Physiology, Kutahya Health Sciences University Faculty of Medicine, Kutahya, Türkiye
[3]Department of Dermatology, Kutahya Health Sciences University Faculty of Medicine, Kutahya, Türkiye

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Address for correspondence:
Fulya Yukcu.
Department of Biophysics, Kutahya Health Sciences University Faculty of Medicine, Kutahya, Türkiye
Phone: +90 274 260 00 43
E-mail: fulya.yukcu@ksbu.edu.tr

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ABSTRACT

Objective: Acne vulgaris (AV) is a common skin disorder. Genotypic variations of antioxidant-related genes may directly influence the function of AV-related genes by mitigating the risk of oxidative stress. This study aimed to investigate the impact of SOD1 +35A/C and GPx-3 +1494A/G gene polymorphisms in patients with AV.

Materials and Methods: The study comprised 81 healthy controls and 81 AV patients. The GPx-3 +1494A/G genotype was evaluated using Allele-Specific Polymerase Chain Reaction (AS-PCR), while the SOD1 +35A/C genotype was analyzed through the Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) technique.

Results: Genotype and allele frequencies of the SOD1 +35A/C gene polymorphism differed significantly between the AV patients and the control group (χ^2=13.9, df=2, p=0.001 and χ^2=13.1, df=1, p=0.001, respectively). Individuals with the AA genotype, compared to those with the AC genotype, showed an increased incidence of AV (Odds Ratio [OR]=4.81, 95% Confidence Interval [CI]=1.94–11.9, p=0.001). Individuals carrying the A allele were at a higher risk of AV compared to those with the C allele (OR=4.43, 95% CI=1.87–10.4, p=0.001). The AC genotype and C allele were associated with a protective effect in the control group (OR=0.21, 95% CI=0.08–0.52, p=0.001 and OR=0.23, 95% CI=0.10–0.54, p=0.001). However, no significant differences were observed in the GPx-3 +1494A/G genotype and allele frequencies between both groups.

Conclusion: The findings of this study indicate a correlation between the SOD1 +35A/C polymorphism and an increased incidence of AV.

Keywords: Acne vulgaris, SOD1 +35A/C, GPx-3 +1494A/G, gene polymorphism, reactive oxygen species.

INTRODUCTION

Acne vulgaris (AV) is a chronic and recurrent condition affecting the sebaceous units of the skin, making it one of the most common issues in clinical dermatology.[1] It ranks as one of the most prevalent dermatological conditions globally, affecting 35% to 90% of teenagers.[2] Multiple etiological factors are known to contribute to the development of AV, including increased sebum production, enhanced keratinocyte proliferation, bacterial colonization of the skin, and chronic inflammation.[3] The occurrence and progression of AV are thought to be influenced by a variety of factors, including environmental, hormonal, immunological, and genetic elements. However, genetic studies have yet to elucidate the precise mechanisms underlying AV.[4]

Key signaling molecules, known as reactive oxygen species (ROS), play a crucial role in the onset of inflammatory disorders.[5] ROS are continuously produced in cells under normal physiological conditions and are counterbalanced by the antioxidative system. The accumulation of superoxide radicals, resulting from the disturbance of this balance and leading to elevated levels of ROS in cells, causes oxidative stress. ROS are harmful to cells and impair lipid and protein metabolism. Increased levels of ROS can disrupt intracellular signaling cascades and have mutagenic effects on deoxyribonucleic acid (DNA).[6]

Superoxide dismutase (SOD) is an essential enzyme required for the elimination of ROS.[7] There are three different SOD isoforms known to exist in mammals: SOD1, SOD2, and SOD3.[8] SOD1, a copper-zinc superoxide dismutase, is present in the cytosol and the mitochondrial intermembrane space. It accounts for between 50% and 80% of all SOD activity, making changes in SOD1 activity the most significant among the SOD isoforms.[9] The SOD1 gene is located in the 21q22 chromosomal region of humans and consists of 5 exons and 4 introns.[10] The +35A/C (rs2234694) gene polymorphism in the SOD1 gene has been studied previously in association with various clinical conditions, including chronic gastritis, type 2 diabetes mellitus, inflammatory bowel disease, age-related macular degeneration, and the development of primary open-angle glaucoma.[6,11–14] However, to our knowledge, there is no study in the literature examining the relationship between the SOD1 +35A/C gene polymorphism and AV.

Plasma glutathione peroxidase (GPx-3), a member of the GPx family that includes selenocysteine, is a critical antioxidant enzyme that neutralizes ROS produced during normal metabolism or in response to oxidative damage.[15] The human GPx-3 gene, approximately 10 kb in length with 5 exons and 4 introns, is located on chromosome 5q32.[16] Studies have explored the relationship between the +1494A/G (rs3828599) gene polymorphism in the GPx-3 gene and conditions such as essential hypertension, type 2 diabetes mellitus, gastric cancer, and thyroid cancer.[16–19] However, there has been no published research on the association between AV and the GPx-3 +1494A/G gene polymorphism.

Genotypic variations in genes related to antioxidants may directly influence the function of genes associated with AV. Individuals carrying such alleles may face an increased risk of lifelong diseases. Therefore, we aimed to examine the effects of the SOD1 +35A/C and GPx-3 +1494A/G gene polymorphisms in patients with AV and to correlate the genotypes identified in these patients with different clinical features of AV.

MATERIALS AND METHODS

Study Cohort

We obtained approval from the Kutahya Health Sciences University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee for our study, with decision number 2023/02-11. In this study, we used DNA samples that had been previously approved for use by the Kutahya Health Sciences University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee. The study involved 81 patients aged 18–65 years who were diagnosed with AV and 81 healthy controls at the Dermatology Clinic of Kutahya Health Sciences University, Evliya Celebi Education and Research Hospital. All participants, both from the healthy control group and the AV patient group, provided signed informed consent.

Determination of Genotypes

GPx3 +1494A/G (rs3828599) Gene Polymorphism

Genotype determination was conducted using the allele-specific polymerase chain reaction (AS-PCR) method with appropriate primers for the GPx3 +1494A/G (rs3828599) gene region.[20] Primer sequences, PCR conditions, and single nucleotide polymorphisms (SNPs) are detailed in Table 1. PCR was performed in a 20 µl volume, including 10 µl of PCR master mix (abm, catalog no: G013, Canada), 100 ng of genomic DNA, 0.4 µl of both forward outer (F0) and reverse outer (R0) primers, and 0.8 µl of both reverse inner (R1) and forward inner (F1) primers (Oligomer, Türkiye). The PCR process utilized a thermal cycler device (Techne, 5PRIMEG/02, Ukraine). PCR products were visualized under ultraviolet light using a gel imaging system (Vilber, Quantum-ST4, France) after 50 minutes of electrophoresis at 130 volts on a 2% agarose gel (Thermo Scientific, EC300XL2, China), allowing genotype determination. Allele names were designated as 347-143 bp for AA, 347-255 bp for GG, and 347-143-255 bp for AG (Fig. 1).

SOD1 +35A/C (rs2234694) Gene Polymorphism

Genotype determination was performed via the PCR method with specific primers for the SOD1 +35A/C (rs2234694) gene region, followed by the Restriction Fragment Length Polymorphism (RFLP) method.[21] Primer sequences, PCR

Table 1. Summary of conditions for SOD1 +35A/C and GPx-3 +1494A/G genetic analyses

	SOD1 +35A/C	**GPx-3 +1494A/G**
Primer sequence (5'3')	Forward primer: 5'-CTA TCC AGA AAA CAC GGT GGG CC-3' Reverse primer: 5'-TCT ATA TTC AAT CAA ATG CTA CAA AAC-3'	Forward outer primer (F0): 5'-TCC CCA ACT CAG AAG GCA TTT TCC A-3' Reverse outer primer (R0): 5'-GGC ATG CCC AGG CTT TCA TTA GC-3' Forward inner primer (F1): 5'-AGT CAG TCC CAA CCT TCA GTT TTG GTA G-3' Reverse inner primer (R1):
Polymerase chain reaction conditions	95 °C for 3 minutes, 35 cycles of 95 °C for 30 seconds, 50 °C for 40 seconds, 72 °C for 1 minute, 72 °C for 5 minutes.	5'-GCC CAA TTG TAT CTT CTT TGA TCT-3' 95 °C for 3 minutes 35 cycles of 95 °C for 30 seconds, 52.9 °C for 40 seconds, 72 °C for 1 minute, 72 °C for 5 minutes.
Polymerase chain reaction size	278 bp	347 bp
Restriction endonuclease incubation conditions	HhaI 37 °C for 16 hours	–
Recognition site	5'…G C G↓C…3' 3'… C↑G C G…5'	–
Fragment length (bp)	AA: 278 bp AC: 278-207-71 bp CC: 207-71 bp	AA: 347-143 bp AG: 347-143-255 bp GG: 347-255 bp

AA: Adenine-adenine; AC: Adenine-cytosine; AG: Adenine-guanine; CC: Cytosine-cytosine.

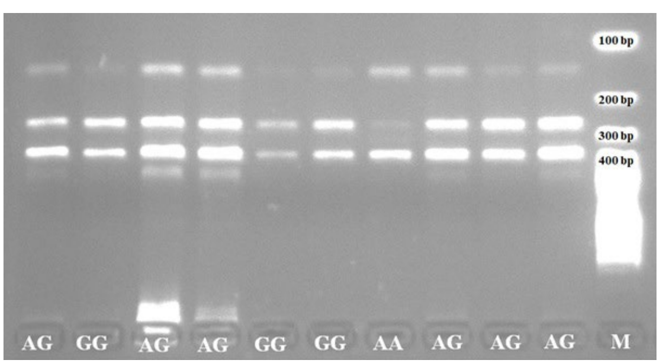

Figure 1. Electrophoresis of the GPx-3 +1494A/G (rs3828599) gene. Product sizes were 143 bp and 347 bp for the AA genotype, 255 bp and 347 bp for the GG genotype, and 143 bp, 255 bp, and 347 bp for the AG genotype.

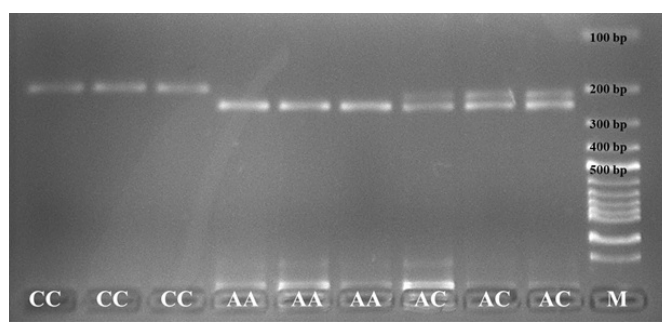

Figure 2. Electrophoresis of the SOD1 +35A/C (rs2234694) gene polymorphism following enzyme digestion. Product sizes were 207 bp for the CC genotype, 207 bp and 278 bp for the AC genotype, and 278 bp for the AA genotype. M: 100 bp DNA molecular weight marker (abm, Catalog No: G193).

conditions, and SNPs are listed in Table 1. The PCR mixture, with a total volume of 20 µl, contained 1.2 µl of both reverse and forward primers (Oligomer, Türkiye), 10 µl of PCR master mix (abm, catalog no: G013, Canada), and 100 ng of genomic DNA sample obtained from peripheral blood. The PCR products, sized at 278 bp, were treated with the HhaI restriction enzyme

Table 2. Clinical characteristics of control and AV groups

Clinical findings	AV (n=81)	Control (n=81)	p
Age	22.4±4.45	–	
BMI	22.3±3.31	–	
Age of onset (years)	17.0±4.17	–	
Gender (n, %)			0.19
Male	25 (32.1%)	34 (42%)	
Female	55 (67.9%)	47 (58%)	
Skin type (n, %)		–	
1	1 (1.2%)		
2	14 (17.3%)		
3	61 (75.3%)		
4	5 (6.2%)		
Acne type (n, %)		–	
Comedonica	9 (11.1%)		
Papulo-pustulosa	54 (66.7%)		
Nodulocystic	18 (22.2%)		
Grading (n, %)		–	
Almost clear	11 (13.6%)		
Mild	24 (29.6%)		
Moderate	31 (38.3%)		
Severe	15 (18.5%)		
Other autoimmune disease (n, %)		–	
Yes	4 (4.9%)		
No	77 (95.1%)		
Family history (n, %)		–	
Yes	35 (43.2%)		
No	46 (56.8%)		

Age, BMI, and age of onset are presented as mean±standard deviation (SD) and were determined by the Independent Student's t-test. Proportions (n, %) were determined by the Pearson Chi-Square (χ^2) test. AV: Acne vulgaris; BMI: Body mass index.

(Thermo, catalog no: ER1851, USA) at 37 °C for 16 hours. These samples were subjected to electrophoresis in a 2% agarose gel (Biomax, catalog no: 000320PR, Türkiye) with 5% ethidium bromide (Bioshop, catalog no: ETB444, Canada). The gel was visualized using an ultraviolet (UV) imaging system (Vilber, Quantum-ST4, France), and the observed bands were evaluated for genotyping. Allele names were designated as 278 bp for AA, 207-71 bp for CC, and 278-207-71 bp for AC (Fig. 2).

Statistical Analysis

The data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software (IBM SPSS Statistics for Windows, Version 20.0, IBM Corp.). The power of the study was determined to be 0.96, a value achieved by collecting 81 samples in each group to analyze the difference between the two independent groups. This calculation was based on a medium effect size of 0.25, a type I error value (alpha) of 0.05, and a type II error value (beta) of 0.05, with a confidence level of 0.95. The calculation was conducted using the G-power 3.1 software, referring to the odds ratio (OR) of 0.35 from the study by Mrowicka M. et al.[13]

The differences in allele and genotype frequencies between the control group and AV patients were compared using the Pearson chi-square (χ^2) test, from which the OR and the 95% confidence interval (95% CI) were derived. The allele and genotype distributions were evaluated for Hardy-Weinberg

Table 3. Hardy-Weinberg equilibrium for SOD1 +35A/C and GPx-3 +1494A/G gene polymorphisms on AV patients and controls

Genotype	Observed	Expected	χ^2	p	Alleles	Frequency
SOD1 +35A/C						
AV (n=81)						
CC	0 (0%)	0.2			C	0.04
AC	7 (21.9%)	6.7	0.16	0.68	A	0.96
AA	74 (57.4%)	74.2				
Control (n=81)						
CC	1 (100%)	2.3			C	0.17
AC	25 (78.1%)	22.5	1	0.31	A	0.83
AA	55 (42.6%)	56.3				
GPx-3 +1494A/G						
AV (n=81)						
GG	21 (52.5%)	29.6			A	0.40
AG	56 (48.7%)	38.7	16.1	0.001*	G	0.60
AA	4 (57.1%)	12.6				
Control (n=81)						
GG	19 (47.5%)	29			A	0.40
AG	59 (51.3%)	38.9	21.5	0.001*	G	0.60
AA	3 (42.9%)	13.0				

Data were analyzed using the Pearson Chi-Square (χ^2) test. *: A p-value <0.05 was considered statistically significant. AA: Adenine-adenine; AC: Adenine-cytosine; AG: Adenine-guanine; AV: Acne vulgaris; CC: Cytosine-cytosine.

equilibrium compliance. The Pearson χ^2 test was utilized to investigate the relationships among categorical variables. Variables adhering to a normal distribution are presented as mean and standard deviation (SD). The comparisons between the groups (AV vs. control) were made using the Independent Student's t-test. The correlation values of clinical parameters between the AV and control groups with SOD1 +35A/C and GPx-3 +1494A/G gene polymorphisms were analyzed using One-Way Analysis of Variance (ANOVA). A significance level of p<0.05 was considered statistically significant.

RESULTS

The Research Population's Clinical Features and Demographics

This study included 81 healthy controls and 81 individuals diagnosed with AV. Demographic and clinical characteristics of the groups participating in the study were analyzed, with the results presented in Table 2. The gender distribution between the control and AV groups was not significantly different (p>0.05). Of the 81 patients, 35 (43.2%) reported a family history of AV. Regarding clinical severity, 13.6% had almost clear acne, 29.6% mild acne, 38.3% moderate acne, and 18.5% severe acne.

Hardy-Weinberg Equilibrium

As shown in Table 3, the expected and observed frequencies of the SOD1 +35A/C gene polymorphism were in Hardy-Weinberg equilibrium for both control and patient groups (p=0.31 and p=0.68). However, the GPx-3 +1494A/G gene polymorphism did not achieve equilibrium (p=0.001).

Genotype and Allele Frequency Distributions

The genotype and allele frequency distributions of the SOD1 +35A/C and GPx-3 +1494A/G gene polymorphisms are detailed in Table 4. No significant difference was observed in the genotype frequencies of the GPx-3 +1494A/G gene polymorphism between the AV and control groups (χ^2=0.321, df=2, p=0.852). The frequencies of the GG, AG, and AA genotypes in the AV group were 52.5%, 48.7%, and 57.1%, respectively, compared to 47.5%, 51.3%, and 42.9% in the control group. Individuals with the AA genotype were 1.40 times more likely to develop AV than those with the AG genotype, although this was not statistically significant (OR=1.40, 95% CI=0.30–6.56, p=0.66). The allele frequencies of the GPx-3 gene +1494A/G polymorphism did not differ significantly between the AV and control groups (χ^2=0.013, df=1, p=0.910).

Table 4. Distribution of SOD1 +35A/C and GPx-3 +1494A/G genotypes and allele frequencies in acne vulgaris patients and controls

Polymorphic site	Control		AV		OR (95% CI)	p	OR (95% CI)	p
	n=81	%	n=81	%				
SOD1 +35A/C								
CC	1	100	0	0	–	–	–	
AC	25	78.1	7	21.9	1 (Reference)	–	0.21 (0.08–0.52)	0.001*
AA	55	42.6	74	57.4	4.81 (1.94–11.9)	0.001*	1 (Reference)	
				χ^2=13.9, df=2, p=0.001*				
C Allele	27	79.4	7	20.6	1 (Reference)	–	0.23 (0.10–0.54)	0.001*
A Allele	135	46.6	155	53.4	4.43 (1.87–10.4)	0.001*	1 (Reference)	
				χ^2=13.1, df=1, p=0.001*				
GPx-3 +1494A/G								
GG	19	47.5	21	52.5	1.16 (0.57–2.39)	0.67	1 (Reference)	–
AG	59	51.3	56	48.7	1 (Reference)	–	0.86 (0.42–1.76)	0.67
AA	3	42.9	4	57.1	1.40 (0.30–6.56)	0.66	1.21 (0.24–6.10)	0.82
				χ^2=0.321, df=2, p=0.852				
G Allele	97	49.7	98	50.3	1.03 (0.66–1.60)	0.91	1 (Reference)	–
A Allele	65	50.4	64	49.6	1 (Reference)	–	0.97 (0.62–1.52)	0.91
				χ^2=0.013, df=1, p=0.910				

Data were analyzed using the Chi-Square (χ^2) test. *: A p-value <0.05 was considered statistically significant. AV: Acne vulgaris; CI: Confidence interval; OR: Odds ratio.

Significant differences were noted in the genotype frequencies of the SOD1 +35A/C gene polymorphism (χ^2=13.9, df=2, p=0.001). The frequencies of the CC, AC, and AA genotypes in the AV group were 0%, 21.9%, and 57.4%, respectively, while in the control group, they were 100%, 78.1%, and 42.6%. Individuals with the AA genotype had a 4.81 times higher risk of developing AV compared to those with the AC genotype (OR=4.81, 95% CI=1.94–11.9, p=0.001). In addition, the AC genotype was more prevalent in the control group and exhibited a protective effect when compared with the AA genotype, which served as a reference (OR=0.21, 95% CI=0.08-0.52, p=0.001). The frequencies of the C and A alleles of the SOD1 +35A/C gene polymorphism were significantly different between the AV (20.6% for C and 53.4% for A) and control groups (79.4% for C and 46.6% for A) (χ^2=13.1, df=1, p=0.001), indicating that the A allele is a significant risk factor for AV (OR=4.43, 95% CI=1.87-10.4, p=0.001). The higher presence of the C allele in the control group provides a protective effect in comparison to the A allele (OR=0.23, 95% CI=0.10–0.54, p=0.001).

No discernible statistical association was observed between the distribution of SOD1 gene +35A/C genotypes (AC and AA) and the clinical and demographic data in AV patients, as shown in Table 5. The AA genotype was found to be more prevalent in women (70.3%) than in men (29.7%). Additionally, the AA genotype was more common than the AC genotype in individuals with a family history of AV and autoimmune diseases. Table 6 indicates that the distribution of GPx3 +1494A/G genotypes (GG, AG, and AA) in AV patients does not significantly correlate with demographic or clinical data.

DISCUSSION

AV is a common chronic inflammatory skin condition that predominantly affects teenagers and young adults.[1] The etiology of acne involves multiple factors, including follicular keratinization, excessive sebum production, the activity of *Cutibacterium acnes*, and inflammation. Moreover, AV has a complex etiology where oxidative stress plays a crucial role.[3] *Cutibacterium acnes* is key in initiating inflammation through the release of substances that attract neutrophils, leading to their accumulation within acne lesions. Neutrophils release ROS, leading to tissue damage.[22] Beyond the toxic effects of ROS, the accumulation of substances like hydrogen peroxide produced by neutrophils is thought to cause additional adverse effects, including inflammation and further tissue damage. Akamatsu et al.[23] observed in their study that individuals with inflammatory acne had significantly higher levels of hydrogen peroxide in their blood compared to healthy individuals.

Table 5. Clinical characteristics of the study population by SOD1 +35A/C genotypes

	SOD1 +35A/C genotypes		
	AC	AA	p
Age	21.7±1.88	22.5±4.62	0.65
BMI	21.7±1.40	22.4±3.44	0.61
Age of onset (years)	18.4±2.69	16.9±4.27	0.36
Gender, n (%)			0.13
Male	4 (57.1%)	22 (29.7%)	
Female	3 (42.9%)	52 (70.3%)	
Skin type, n (%)			0.80
1	0 (0%)	1 (1.4%)	
2	1 (14.3%)	13 (17.6%)	
3	5 (71.4%)	56 (75.6%)	
4	1 (14.3%)	4 (5.4%)	
Acne type, n (%)			0.33
Comedonica	1 (14.3%)	8 (10.8%)	
Papulo-pustulosa	3 (42.9%)	51 (68.9%)	
Nodulocystic	3 (42.9%)	15 (20.3%)	
Grading, n (%)			0.16
Almost clear	0 (0%)	11 (14.9%)	
Mild	3 (42.9%)	21 (28.4%)	
Moderate	1 (14.3%)	30 (40.5%)	
Severe	3 (42.9%)	12 (16.2%)	
Autoimmune disease, n (%)	1 (25%)	3 (75%)	0.23
Family history, n (%)	2 (5.7%)	33 (94.3%)	0.41

Age, BMI, and age of onset are presented as mean±standard deviation (SD) and were determined by the Independent Student's t-test. Proportions (n, %) were determined by the Pearson Chi-Square (χ^2) test. *: A p-value <0.05 was considered statistically significant. AA: Adenine-adenine; AC: Adenine-cytosine; BMI: Body mass index.

Table 6. Clinical characteristics of the study population by GPx-3 +1494A/G genotypes

	GPx-3 +1494A/G genotypes			
	GG	AG	AA	p
Age	24.0±6.33	21.9±3.53	20.5±2.08	0.11
BMI	22.2±3.74	22.5±3.22	21.3±2.79	0.78
Age of onset (years)	17.1±4.88	17.0±3.97	15.7±3.59	0.81
Gender, n (%)				0.28
Male	4 (19%)	21 (37.5%)	1 (25%)	
Female	17 (81%)	35 (62.5%)	3 (75%)	
Skin type, n (%)				0.09
1	0 (0%)	1 (1.8%)	0 (0%)	
2	3 (14.3%)	8 (14.3%)	3 (75%)	
3	16 (76.2%)	44 (78.6%)	1 (25%)	
4	2 (9.5%)	3 (5.4%)	0 (0%)	
Acne type, n (%)				0.52
Comedonica	2 (9.5%)	6 (10.7%)	1 (25%)	
Papulo-pustulosa	16 (76.2%)	35 (62.5%)	3 (75%)	
Nodulocystic	3 (14.3%)	15 (26.8%)	0 (0%)	
Grading, n (%)				0.21
Almost clear	2 (9.5%)	8 (14.3%)	1 (25%)	
Mild	7 (33.3%)	14 (25%)	3 (75%)	
Moderate	10 (47.6%)	21 (37.5%)	0 (0%)	
Severe	2 (9.5%)	13 (23.2%)	0 (0%)	
Autoimmune disease, n (%)	1 (25%)	3 (75%)	0 (0%)	0.89
Family history, n (%)	9 (25.7%)	25 (71.4%)	1 (2.9%)	0.74

Age, BMI, and age of onset are presented as mean±standard deviation (SD) and were determined by ANOVA. Proportions (n, %) were determined by the Pearson Chi-Square (χ^2) test. *: A p-value <0.05 was considered statistically significant. AA: Adenine-adenine; AG: Adenine-guanine; BMI: Body mass index; GG: Guanine-guanine.

The follicular wall becomes a target of neutrophil-induced ROS assault and subsequent lipid peroxidation, leading to its destruction. This destruction triggers the expression and release of pro-inflammatory ingredients such as interleukin-1 (IL-1), tumor necrosis factor (TNF) alpha, and interleukin-8 (IL-8).[24,25] IL-1, for example, can stimulate endothelial cells and polymorphonuclear leukocytes to release ROS. This cascade of events initiates further alterations and damage in the architecture of surrounding tissues, exacerbating inflammation.[26] The pathogenesis of skin disorders, including acne, may be significantly influenced by oxidative stress and imbalances in antioxidant equilibrium. The body produces antioxidants as a defense mechanism against free radicals, utilizing enzymes like glutathione peroxidase, catalase, and SOD.[27] Antioxidative enzymes exhibit polymorphism, leading to individual variability in the genetic phrase of the enzymes encoded by these genes, which arises from genetic diversity. SNPs in antioxidant enzyme genes such as SOD and GPx-3 can result in individual gene variants.[28]

The SOD1 gene contains 5 exons, and the +35A/C polymorphism is located near the splice site (exon3/intron3).[9] In one study, increased SOD1 activity was observed in diabetic patients with the AA genotype.[29] Another study linked the SOD1 + 35A/C gene polymorphism, C allele frequency, and AC genotype to protection against age-related macular degeneration in the Polish population.[13] Advanced stages of diabetic nephropathy have been associated with the mutant C allele of the rs2234694 polymorphism in the SOD1 gene in a Romanian study of individuals with type 1 diabetes.[30] Ferroni et al.[31] found no statistically significant difference in allele frequencies and genotype for the SOD1 rs2234694 polymorphism between control and patient groups in their study on migraine patients. However, they observed that white matter hyperintensities in migraine patients were associated with Magnetic Resonance Imaging (MRI) findings and the SOD1 rs2234694 C allele. A study conducted on a South Indian population, including patients with type 2 diabetes, type 1 diabetes patients, and healthy individuals with no family history of diabetes, concluded that the CC and AC genotypes were absent in both the control and type 2 diabetes mellitus patient groups. Furthermore, the A allele was more prevalent in diabetic patients than in the control group.[11] Another study revealed that the North Indian population lacked both the C allele and CC genotypes, showing no correlation between the SOD1 +35A/C gene polymorphism and diabetes.[32] In research involving Turkish women with polycystic ovary syndrome, the CC genotype was not found in either the control or patient groups for the SOD1 +35A/C gene polymorphism, while the AA genotype occurred at a higher frequency in patients, although the study did not find this difference to be significant.[33]

To date, there is no source in the literature investigating the association between the SOD1 +35A/C gene polymorphism and AV. This study represents the first investigation into the relationship between the GPx-3 +1494A/G and SOD1 +35A/C gene polymorphisms and AV in the Turkish population. The distribution of SOD1 gene +35A/C polymorphism genotypes and allele frequencies revealed statistically significant differences between the AV and control groups. A noteworthy increase in the A allele and AA genotype was observed when comparing the AV group to the control group. The different results observed in the SOD1 + 35A/C gene polymorphism suggest that the study participants might come from different ethnic backgrounds.

GPx-3, the only antioxidant enzyme that functions extracellularly, is one of the most important antioxidant enzymes present in plasma.[34] It catalyzes the reduction of lipid peroxides, hydrogen peroxide (H_2O_2), and organic hydroperoxides, thereby protecting cells and enzymes from oxidative damage.[35] Despite the recognized importance of oxidative damage in AV, no study in the literature has explored the connection between AV and GPx-3 gene polymorphism. In one study, the GG genotype of the rs3828599 polymorphism of the GPx-3 gene was associated with hypertension.[36]

Limitations

Our study has a few limitations. Firstly, it includes only a small number of subjects, as genotypic analysis is costly. Secondly, we did not measure serum levels of SOD and GPx-3 in patients with AV. As a result, we could not compare blood SOD and GPx-3 levels with the SOD1 +35A/C and GPx3 +1494A/G gene polymorphisms. Further research is required to confirm these polymorphism findings with serum antioxidant enzyme levels in individuals with AV.

CONCLUSION

In conclusion, an imbalance between antioxidants and oxidative stress may play a significant role in the development and progression of skin disorders. Despite the prevalence of acne vulgaris, there is a lack of research on antioxidative systems in its pathophysiology. We cannot compare our findings to any published research because there is no research on the association between AV and the SOD1 +35A/C and GPx3 +1494A/G gene polymorphisms. Our findings suggest a relationship between the +35A/C polymorphism of the SOD1 gene and AV in the Turkish population, indicating that individuals with acne vulgaris are at increased risk for the AA genotype and the A allele of the SOD1 +35A/C gene polymorphism. To fully understand the role of antioxidants in the molecular pathways related to skin disorders, in-depth exploration into the molecular mechanisms and identification of various oxygen species involved in these conditions are required. This knowledge lays the groundwork for developing treatment approaches. Therefore, our research is expected to serve as a valuable resource for future studies. This enhances the originality of our work and the further investigation we plan to undertake on this topic.

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