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Survivin Gene Polymorphism in Association with Plasma Survivin Level as Potential Risk Factors for Acne Severity and Post-Acne Scaring

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ABSTRACT

Background: Acne vulgaris is the most common cutaneous ailment in the world, affecting up to 80% of teenagers and up to 50% of adults. It is a chronic inflammatory disease of the pilosebaceous unit. The development of acne lesions is heavily influenced by keratinocyte proliferative and inflammatory states, which have been observed to elevate survivin levels.

Objective: This study was conducted to assess survivin gene polymorphism and its plasma level in patients with active acne vulgaris and patients with post acne scars with varying severity.

Patients and methods: The study included 60 acne patients divided into two groups: 30 patients with active acne lesions and 30 patients with post acne scars; in addition to 30 healthy volunteers who were served as control group selected from Outpatient Clinic, Department of Dermatology, Andrology and STD, Mansoura University Hospitals, Mansoura, for 1 year duration.

Results: The levels of serum survivin in both group of patients with active acne and group of patients with post acne scars are significantly higher than that of the control group. There was no statistically significant difference in the serum survivin levels among the patients with different grades of acne. There was a significant increase in the serum survivin level with increased severity of post-acne scars. The distribution of the survivin rs-9904341 & rs-1042489 genotypes among the study's groups did not differ significantly ($P > 0.05$) for each.

Conclusion: It could be concluded that survivin may be used as a diagnostic biomarker in acne vulgaris and as a prognostic tool for post acne scarring severity. Survivin is involved in the pathogenesis of active acne vulgaris and more importantly, the pathogenesis of the development of fibrotic tissue in acne scars.

Keywords: Acne, Survivin gene polymorphism, Plasma Survivin level.

INTRODUCTION

The most typical time for the development of acne vulgaris, a pilosebaceous unit illness, is during adolescence. The severity of the condition varies from person to person. Over 650 million individuals, or 9.4% of the world's population, are impacted. While acne vulgaris is the most prevalent illness in adolescents, little has been published regarding its complex pathogenesis [1]. Acne vulgaris is caused by a variety of variables, including genetics, food, hormones, stress, and environment [2]. According to its intensity, acne may be split into three groups: mild, moderate, and severe. Papules, pustules, nodules, and cysts are examples of classifications for both inflammatory and non-inflammatory disorders [3].

The family of genes known as apoptotic inhibitors includes the human survivin gene. The roles of transcription factors are reportedly impacted by single nucleotide polymorphism of the survivin promoters, which changes how proteins are expressed [4]. Survivin is expressed at relatively high levels in a range of malignant tissues, embryonic and fetal tissues, as well as a small number of normal adult tissues, including skin. Normal tissues either do not express survivin or do so at extremely low levels [5].

Atypical apoptosis and increased sebocyte survival mediated by survivin may both have an impact on infundibular keratinocyte differentiation and altered sebum production, which can result in comedones and acne [6]. According to **El-Tahlawi *et al.*** [7] study on the Egyptian population, there were statistically significant differences in the levels of survivin and IGF-I in the control and sick groups. In light of this, Survivin and IGF-I could contribute to the pathogenesis of both active acne and the formation of postinflammatory acne scars [8].

This study was conducted to assess survivin gene polymorphisms and its level in plasma of patients with acne vulgaris of varying severity with and without post-acne scarring.

SUBJECTS AND METHODS

This case-control study included a total of 60 acne patients, attending at Outpatient Clinic, Department of Dermatology, Andrology and STD, Mansoura University Hospitals, Mansoura.

The patients were divided into two groups where **group (A)** included 30 patients with acne vulgaris without post acne scars, **group (B)** included 30 patients with acne and post acne scars. In addition to **control group** that included 30 healthy persons who were age and gender matched with the patients.

Inclusion criteria: Patients with acne vulgaris of varying severity with or without post acne scar who were aged from 13 to 35 years, and did not receive any

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systemic medical treatment for acne in the past 3 months were included.

Exclusion criteria: Patients with history of acute or chronic liver disease, history of acute or chronic kidney disease, history of malignancy, and history of any other cutaneous or fibrotic disease we excluded. Also, pregnant, and lactating women were excluded.

The medical records of patients were reviewed using computerized sheet including all studied data for each patient that included:

- Personal data such as name, age, gender, occupation, residence.
- History of the present illness: onset, course, duration of the disease.
- Family history of acne vulgaris or other dermatomes.
- Previous medical history and current treatment.
- Past history of any associated systemic (liver, renal and cardiac diseases), dermatological diseases or major surgical operations.

All patients were also subjected to complete general examination to exclude any systemic or other skin diseases. The Body Mass Index (BMI) was also estimated for each patient.

Using the global acne grading system, an inspection of the acne lesions was conducted to determine the type, distribution, and severity of the lesions (GAGS) [9]. The face, chest, and upper back are divided into six categories using this grading system. GAGS the location factors are as follows: the forehead factor is 2, the right cheek is 2, the left cheek is 2, the nose is 1, the chin is 1, and the chest and upper back are 3. No lesion was graded as 0, comedones were graded as 1, papules were graded as 2, pustules were graded as 3, and nodules were graded as 4. The most severe lesion is multiplied by the area factor to determine the score for each location (Local score). [Local score = Grade (0–4) location factor]. The total score, which ranges from 0 (no acne) to 1–38 (severe acne), is the product of all local scores. The Goodman and Baron scaring grade method was applied in the instance of the post-acne scar [10].

Assessment of serum survivin using ELISA

Six milliliters (6 ml) of venous blood sample was withdrawn from all subjects and divided into 2 EDTA containing tubes. One tube was used for separation of plasma for survivin protein assay using ELISA kit (Catalog No. E-EL-H158496T) according to manufacturer's instruction.

Genomic DNA extraction and survivin genotyping

As directed by the manufacturer, the Spin column technique was employed to extract DNA from whole blood (Scientific Zymo Bead Genomic DNA Kits, Quick-g DNA Mini Prep, Murphy Ave. Irvine, CA, U.S.A). The genomic DNA that had been eluted was kept at -80°C until PCR amplification. A PCR reaction utilizing commercially available kits and gene-specific primers was used to evaluate the survival gene, and Mspl enzyme was used to identify Restriction Fragment Length Polymorphism (RFLP). The PCR-restriction fragment length polymorphism technique was used to assess the genotype and allele frequency distribution of the survivin single-nucleotide gene polymorphisms.

Ethical consideration:

This study was ethically approved by Mansoura University Research Ethics Committee. Written informed consent of all the participants was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

Data were entered into the computer and analyzed using the IBM SPSS software programme version 20.0. IBM Corporation, Armonk, New York. To describe qualitative data, numbers and percentages were employed. The Shapiro-Wilk test was used to determine the distribution's normality. To describe quantitative data, the terms range, mean, standard deviation, median, and interquartile range were employed (IQR). The qualitative data was shown using frequency tables (Number and percentages). Quantitative variables included Before the data were shown by central indices and dispersion, the Shapiro-Wilk test was employed to establish their normality: Mean Standard deviation for variables with a normal distribution (SD). The chi-square test was used to compare various groups for categorical data. The Monte Carlo method must be used to adjust Chi-square when more than 20% of the cells have an anticipated count that is less than 5. In order to compare two groups for quantitative traits that were not regularly distributed, the Mann Whitney test was utilized. In order to compare more than two research groups utilizing quantitative variables that were not normally distributed, the Kruskal Wallis test and the Post Hoc (Dunn's multiple comparisons test) were utilized. Quantitative variables having Hardy-Weinberg distributions that are regularly distributed were compared across more than two groups using the F-test (ANOVA). The Hardy-Weinberg equation was also utilized to determine the population's equilibrium for the examined sample. The 5% threshold of significance was applied to the findings (P 0.05).

RESULTS

This case-control study was conducted on three groups. The first group (A) included 30 patients with acne lesions; the second group (B) included 30 patients with post-acne scars and control group including 30 normal matched subjects.

Table (1) demonstrates demographic data analysis for the studied groups. The group of patients

with acne lesions (Group A) included 7 male patients (23.3%) and 23 female patients (76.6%), the group of patients with post-acne scars (Group B) included 9 male patients (30%) and 21 female patients (70%) whereas the healthy control group included 10 males (46.7%) and 20 females (53.3%).

The subjects average age for group A was (22.8 ± 4.7) ranged from 13.0 to 29.5 years, for group B was (26.9 ± 5.0) ranged from 21.5 to 35.0 years, for control group was (25.2 ± 5.3) ranged from 14.0 to 34.5 years.

There were no statistically significant differences between the patient groups and control group regarding gender and age. However, the result showed a significant increase in the marital status in group B compared to group A. This can be interpreted according to the higher range of age of post acne scars patients as compared to that of the patients with acne **(Table 1)**.

The body mass index (BMI) range in the group of patients with acne lesions was 20.60 to 29.40 kg/m² with a mean of 24.02 ± 2.29 kg/m², in the group of patients with post acne scars was 20.60 to 31.20 kg/m² with a mean of (25.23 ± 3.06 kg/m²) and in the control group was 20.50 to 31.20 kg/m² with a mean of (25.09 ± 2.87 kg/m²). Between the studied groups, there were no statistically significant differences in BMI. There was no statistically significant difference in the smoking status between the patient groups and the control healthy group **(Table 1)**.

Table (1): Analysis of demographic data of the three studied groups, BMI and state of obesity and Smoking (group with acne lesions (Group A), group with post acne scars (Group B) and the control group

	Group A (n = 30)		Group B (n = 30)		Control group (n = 30)		Test of significance
	No.	%	No.	%	No.	%	
Gender							
Male	7	23.3	9	30.0	10	53.3	$\chi^2 = 0.498$
Female	23	76.7	21	70.0	20	46.7	**P** = 0.339
Age (years)							
Min. – Max.	13.0 – 29.5		21.5 – 35.0		14.0 – 34.5		**H** = 27.451
Mean ± SD.	22.8 ± 4.7		26.9 ± 5.0		25.2 ± 5.3		**P** = 0.081
Marital status							
Single	24	80.0	12	40.0	14	46.7	$\chi^2 = 11.16^*$
Married	6	20.0	18	60.0	16	53.3	**P** = 0.004*
Obesity							
Non-obese (<25)	19	63.3	16	53.3	17	56.7	$\chi^2 = 0.638$
Obese (>25)	11	36.7	14	46.7	13	43.3	**P** = 0.727
BMI (kg/m²)							
Min. – Max.	20.60 – 29.40		20.60 – 31.20		20.50 – 31.20		**F** = 1.721
Mean ± SD.	24.02 ± 2.29		25.23 ± 3.06		25.09 ± 2.87		**P** = 0.185
Smoking							
Non-Smoker	28	93.3	27	90.0	24	80.0	χ^2 = 2.446
Smoker	2	6.7	3	10.0	6	20.0	$^{MC}P = 0.369$

χ^2: Chi square test

H: H for Kruskal Wallis test, Pairwise comparison between each 2 groups was done using Post Hoc Test.

MC: Monte Carlo; *: Statistically significant at $p \leq 0.05$

Table **(2)** shows that the post-acne scars patients had a significant increase ($P < 0.05$) in the positive family history for acne rather than that of patients with acne lesions.

Table (2): Comparison of patients' groups according to the family history for acne

	Group A (n = 30)		Group B (n = 30)		Test of significance
	No.	%	No.	%	
Family history					
Negative	17	56.7	8	26.7	$\chi^2 = 5.554$
Positive	13	43.3	22	73.3	P = 0.018*
Duration (years)					U = 88.0
Mean ± SD	2.61 ± 2.22		9.38 ± 4.95		P <0.001*

χ^2: Chi square test; U: Mann Whitney test; SD: Standard deviation; *: Statistically significant at $p \leq 0.05$

The distribution of acne severity in the acne patients' group (group A) according to GAGS grading system were 70%, 20% and 10% for mild, moderate and severe, respectively **(Figure 1)**.

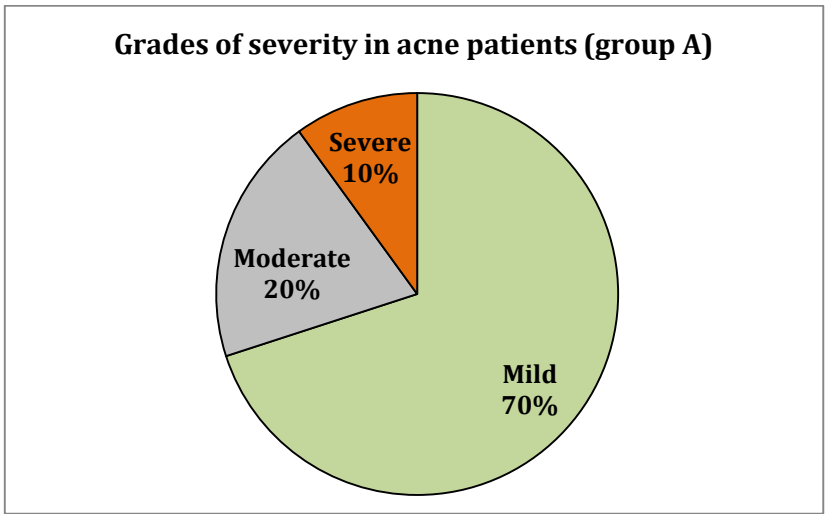

Figure (1): Grades of severity in acne patients (group A) according to GAGS grading system

By applying Goodman grading system on the group of patients with post acne scars (group B), result revealed that moderate affection was the most common form (43.3%), followed by mild affection (33.3%) and severe affection (23.3%) (**Figure 2).**

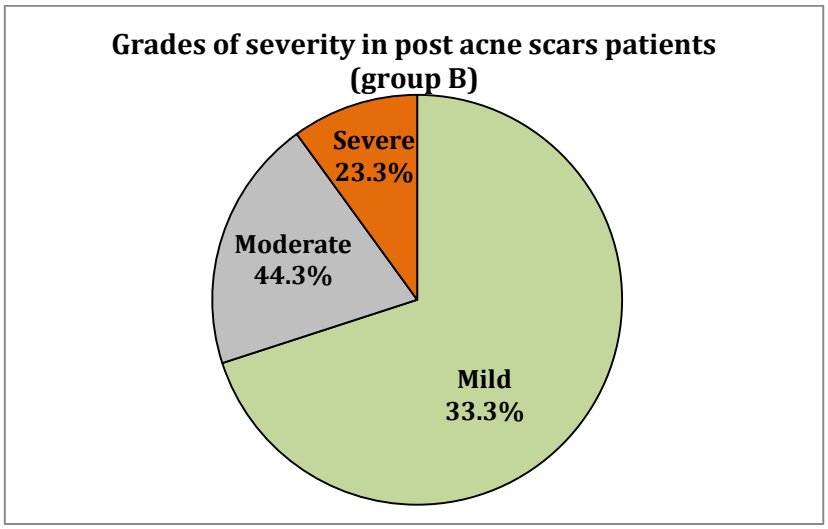

Figure (2): Grades of severity in post acne scar patients (group B) according to Goodman grading system

Figure (3) shows that the levels of serum survivin in both group A (41.3 ± 11.3 pmol/ml) and group B (55.8 ± 27.6 pmol/ml) are significantly higher than that of the control group (30.5 ± 5.7 pmol/ml). Meanwhile, there is no statistically significant difference between the group of patients with acne and the group of patients with post acne scars as regard level of serum survivin.

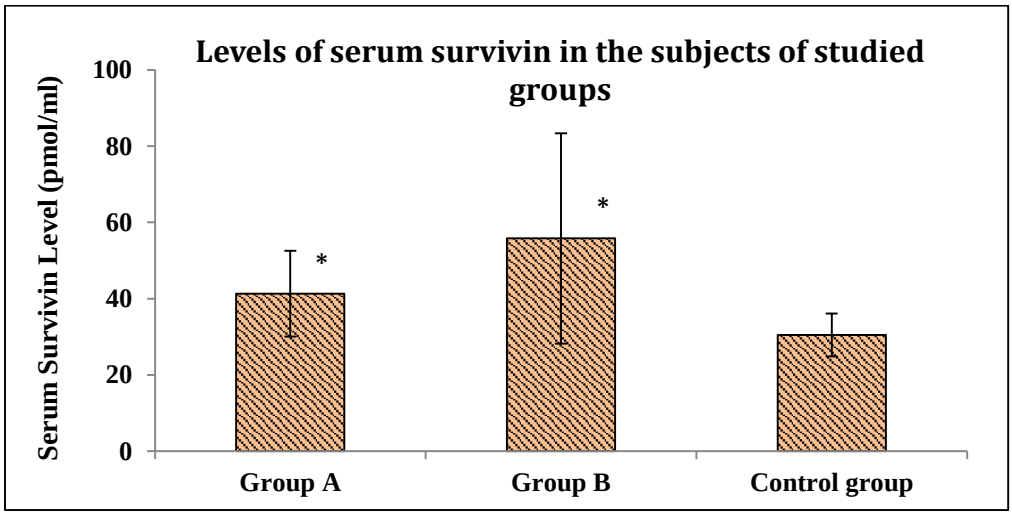

Figure (3): Levels of serum survivin in the subjects of studied groups

As shown in **figure (4),** the level of serum survivin in patients with mild, moderate and severe acne are 38.9, 49.5 and 41.6 pmol/ml, respectively. Results showed that there are no statistically significant differences in the serum survivin levels among patients with various grades of acne.

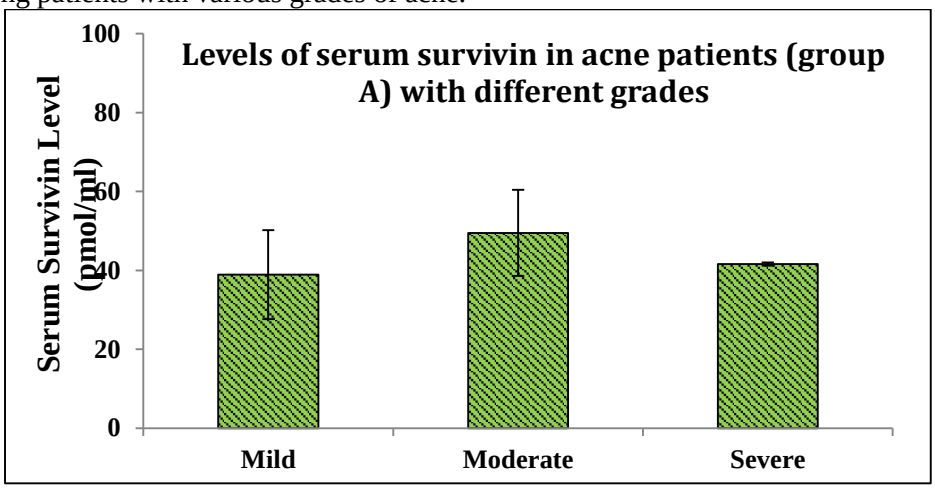

Figure (4): Levels of serum survivin in patients with different grades of acne (group A)

Figure (5) shows that the levels of serum survivin in patients with mild, moderate and severe post-acne scars are 36.7, 48.0 and 97.5 pmol/ml, respectively. Results revealed that there is a significant increase in the serum survivin level with increased severity of post-acne scars ($P < 0.005$).

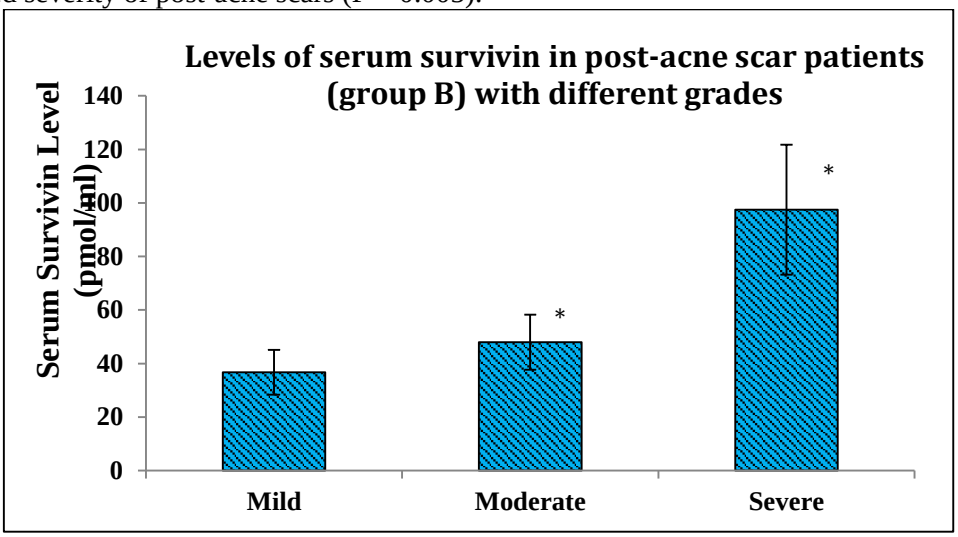

Figure (5): Levels of serum survivin in patients with different grades of post acne scars (group B)

Table **(3)** shows that there was no statistically significant difference in the serum survivin levels between different polymorphisms of rs-9904341 gene in group (A) and group (B).

Table (3): Relation between serum survivin levels and rs-9904341 gene polymorphism in group (A) and group (B)

	Frequency (%)	Serum Survivin Level (pmol/ml)	Test of significance
Group A			
GG	43.3	42.2 ± 10.4	P1 = 0.756
CG	33.3	37.5 ± 8.5	P2 = 0.593
CC	23.4	45.1 ± 11.1	P3 = 0.632
Group B			
GG	66.6	56.2 ± 13.6	P1 = 0.153
CG	26.7	56.1 ± 13.4	P2 = 0.591
CC	6.7	50.2 ± 9.3	P3 = 0.652

P1, P2 and P3 indicate significance changes in survivin level between GG & GC, GG & CC and GC & CC, polymorphisms, respectively.

Table **(4)** shows that there was no significant difference between group A and group B as regard serum survivin levels in different polymorphisms of rs-1042489 gene

Table (4): Relation between serum survivin levels and rs-1042489 gene polymorphism in group (A) and group (B)

	Frequency (%)	Serum Survivin Level (pmol/ml)	Test of significance
Group A			
TT	50.0	42.0 ± 10.2	P1 = 0.593
TC	36.7	37.0 ± 8.0	P2 = 0.346
CC	13.3	50.5 ± 12.4	P3 = 0.588
Group B			
TT	33.3	58.5 ± 14.3	P1 = 0.193
TC	40.0	49.1 ± 12.3	P2 = 0.539
CC	26.7	62.4 ± 15.2	P3 = 0.190

P1, P2 and P3 indicate significance changes in survivin level between TT & TC, TT & CC and TC & CC, polymorphisms, respectively.

Table (5) shows the distribution of rs-9904341 polymorphisms among the different grades of acne vulgaris. Results revealed that there was no significant difference in the distribution of rs-9904341 polymorphism among the different grades of acne patients.

Table (5): Frequency of survivin genotype polymorphism rs-9904341 in patients with different grades of acne (group A)

rs-9904341 Polymorphism	Acne patients (Group A)			Significance
	Mild (n=21)	Moderate (n=6)	Severe (n=3)	
GG	9 (42.9%)	3 (50.0%)	1 (33.3%)	$^{MC}p_1$=0.121
CG	7 (33.3%)	1 (16.7%)	2 (66.7%)	$^{MC}p_2$=0.132
CC	5 (23.8%)	2 (33.3%)	0 (0.0%)	$^{MC}p_3$=0.156
$^{HW}\chi^2$ (p)	0.801 (0.494)	0.733 (0.461)	0.624 (0.485)	

MC: Monte Carlo; $^{HW}\chi^2$: Chi square for goodness of fit for Hardy-Weinberg equilibrium
P1, P2 and P3: P values for comparing between GG, CG and CC frequencies among different severities of post-acne scar patients, respectively.

Table (6) shows that in patients with different grades of post-acne scars, there is no statistically significant difference in the genotype distribution of the rs-9904341 polymorphisms.

Table (6): **Frequency of survivin genotype polymorphism rs-9904341 in patients with different grades of post-acne scars (group B)**

rs-9904341 Polymorphism	Post-acne scars patients (Group B)			Significance
	Mild (n=10)	Moderate (n=13)	Severe (n=7)	
GG	9 (90.0%)	6 (46.1%)	5 (71.4%)	$^{MC}p_1$=0.103
CG	1 (10.0%)	5 (38.5%)	2 (28.6%)	$^{MC}p_2$=0.112
CC	0 (0.0%)	2 (15.4%)	0 (0.0%)	$^{MC}p_3$=0.166
$^{HW}\chi^2$ (p)	0.81 (0.203)	1.07 (0.382)	0.31 (0.624)	

MC: Monte Carlo; $^{HW}\chi^2$: Chi square for goodness of fit for Hardy-Weinberg equilibrium
P1, P2 and P3: P values for comparing between GG, CG and CC frequencies among different severities of post-acne scar patients, respectively.

Table (7) shows the distribution of rs-1042489 polymorphisms among the different grades of acne vulgaris. Results revealed that there was no significant difference in the distribution of rs-1042489 polymorphism among the different grades of acne patients.

Table (7): Frequency of survivin genotype polymorphism rs-1042489 in patients with different grades of acne (group A)

rs-1042489 Polymorphism	Acne patients (Group A)			Significance
	Mild (n=21)	Moderate (n=6)	Severe (n=3)	
TT	10 (47.6%)	4 (66.6%)	1 (33.3%)	$^{MC}p_1$= 0.415
TC	8 (38.1%)	1 (16.7%)	2 (66.7%)	$^{MC}p_2$= 0.524
CC	3 (14.3%)	1 (16.7%)	0 (0.0%)	$^{MC}p_3$= 0.638
$^{HW}\chi^2$ (p)	0.81 (0.203)	1.07 (0.382)	0.31 (0.624)	

MC: Monte Carlo; $^{HW}\chi^2$: Chi square for goodness of fit for Hardy-Weinberg equilibrium
P1, P2 and P3: P values for comparing between TT, TC and CC frequencies among different severities of post-acne scar patients, respectively.

Table (8) shows that in patients with different grades of post-acne scars, there is no statistically significant difference in the genotype distribution of the rs-1042489 SNPs.

Table (8): Frequency of survivin genotype polymorphism rs-1042489 in patients with different grades of post-acne scars (group B)

rs-1042489 Polymorphism	Post-acne scars patients (Group B)			Significance
	Mild (n=10)	Moderate (n=13)	Severe (n=7)	
TT	2 (20.0%)	4 (30.8%)	4 (57.1%)	$^{MC}p_1$= 0.415
TC	6 (60.0%)	5 (38.4%)	1 (14.3%)	$^{MC}p_2$= 0.524
CC	2 (20.0%)	4 (30.8%)	2 (28.6%)	$^{MC}p_3$= 0.638
$^{HW}\chi^2$ (p)	0.81 (0.203)	1.07 (0.382)	0.31 (0.624)	

MC: Monte Carlo; $^{HW}\chi^2$: Chi square for goodness of fit for Hardy-Weinberg equilibrium
P1, P2 and P3: P values for comparing between TT, TC and CC frequencies among different severities of post-acne scar patients, respectively.

DISCUSSION

Regarding age, sex, and body mass index, there were no statistically significant differences between the studied groups in the current study. The group of patients with acne lesions (group A) included 7 (23.3%) males and 23 (76.7%) females with ages ranging from 13.0 to 29.5 years with a mean of 22.8 ± 4.7 years and the body mass index (BMI) ranged from 20.60 to 29.40 kg/m² with a mean of 24.02 ± 2.29 kg/m². Meanwhile, the group of patients with post-acne scars (group B) included 9 (30.0%) males and 21 (70.0%) females with ages ranging from 21.5 to 35.0 years with a mean of 26.9 ± 5.0 years and the BMI ranged from 20.60 to 31.20 kg/m² with a mean of 24.02 ± 2.29 kg/m².

Similar with the average age of the acne patients in the current study (group A), the results of **Assaf *et al.* [8] and Mazzetti *et al.* [11]** indicated that for acne vulgaris patients the average mean ages were 24.0±7.1 and 24.4±7.3 years respectively. These researches involved acne patients from Egypt and Italy who resided in the Mediterranean area, where our study's socioeconomic and climatic settings were similar.

Also, our findings showed that patients with post-acne scars are older than patients with acne, with a mean age of 26.9±5.0 years. This finding was consistent with that of **Assaf *et al.* [8],** who found that patients with post-acne scars tend to be older than those with acne vulgaris. Moreover, our results were consistent with those of **Chuah and Goh [12],** who stated that the mean average age of study participants with post-acne scars was 25.1±4.8 years.

The results of the current study revealed that the frequency of acne was more in females rather than that in males. Similar findings were reported by **Sevimli [13],** who studied Turkish acne patients with a female to male ratio of around 2.2:1. An earlier study found that Asians have a male to female acne prevalence ratio of roughly 1: 1.1 to 1.25 **[10]**. Moreover, it had been shown that Taiwanese women were more likely than men to experience acne and its accompanying illness load, with a ratio of (M: F = 1/1.5-1.9) **[15]**.

Females may experience more acne outbreaks due to hormonal changes during menstruation or increased levels of stress **[16]**. Contrarily, according to **Kaushik *et al.* [17]**, men had twice as much acne as women did. These results might be the outcome of variances in the sampled population's characteristics or the nation under inquiry **[18]**. This conclusion may be explained by the fact that girls seek therapy more frequently than boys and are more conscious of their facial features. In comparison to males, women felt more embarrassed, were more concerned about the illness, and sought medical attention more frequently. Women are also more emotional and sensitive about their looks and the possible impact of the condition on their marital status, as well as more conscious of the attractiveness of their skin.

In terms of BMI, there was no statistically significant difference between acne sufferers and controls. However several studies have shown that those who are overweight or obese—typically characterized as having a BMI ≥23 kg/m2 and ≥ 25

kg/m2, respectively—had greater incidences of acne than those who are underweight (BMI <18.5 kg/m2) or normal weight (18.5 kg/m2 BMI < 23 kg/m2) [18, 19]. In general, androgen and glycemic loads are greater in obese and overweight adults, which may enhance sebum production and promote the growth of acne lesions [20].

In the current study, there was no significant difference between the acne patients and control healthy individuals in the smoking status. The clinical report on the relationship between smoking and acne is currently controversial. Previous research has shown that smoking can make acne worse, but other studies have refuted this claim and even found preventive effects [21]. A comprehensive study and meta-analysis on the connection between acne and smoking was carried out by **Mannocci *et al.*** [22]. There was no discernible link between smoking and the development of acne. In a related study, **Zhang *et al.*** [23] discovered that smokers, particularly men, have an increased chance of developing acne. Similarly, **AlHussein *et al.*** [24] found a strong positive connection between smoking and the severity of acne (P=0.002). Yet, their analysis showed that the acne groups had a higher proportion of smokers.

In the current study, 43.3% of the group of patients with acne lesions had positive family history of acne vulgaris. Interestingly, 73.3% of the group of patients with post-acne scars have positive family history of acne vulgaris with a significant difference between the two patient groups (P = 0.018). According to **El-Tonsy *et al.*** [25] found that 33% of AV patients had positive acne scars, and that patients with a positive family history of acne were more likely to have post-acne scars (55.7%) than those with a negative family history. On the other hand, a post-acne scar is likely to develop in roughly 21.2% of patients with no known family history of acne (P = 0.001).

In the current study, patients with post-acne scars had a significantly longer mean acne duration (9.38±4.95 years) than patients with simply an acne lesion (2.61±2.22 years) (P 0.001). Acne is frequently a chronic disorder that changes in distribution and intensity and need for long-term care. It has been seen to last into adulthood in up to 50% of people despite therapy. The WHO definition of chronic illness [26], is consistent with this trend. The relationship between the length of acne and the development of scars suggests that early treatment of inflammatory acne would significantly reduce the risk of both physical and psychological scarring [27, 28].

Results of the current study showed that the levels of serum survivin in both acne patients (41.3 ± 11.3 pmol/ml) and post-acne scars patients (55.8 ± 27.6 pmol/ml) were significantly higher than that of the control group (30.5 ± 5.7 pmol/ml) (P<0.001 for both). Meanwhile, there was no significant difference between the two groups of acne patients (P=0.453). Meanwhile, the average levels of serum survivin in the mild, moderate and severe acne patients were 38.9, 49.5 and 41.6 pmol/ml, respectively. There were no statistically significant differences in the serum survivin levels among the different grades of acne patients. Also, the average levels of serum survivin in the mild, moderate and severe post-acne scar patients were 36.7, 48.0 and 97.5 pmol/ml, respectively. There was a significant increase in the serum survivin level with increased severity of post-acne scars.

Like our results, **Assaf *et al.*** [8] stated that serum levels of survivin were considerably greater in the groups with active acne (p 0.05) and acne scars (p 0.001) compared to the healthy control group. Western blotting tests showed that the acne scar group expressed more survivin than the control group or the acne group with active acne.

El-Tahlawi *et al.* [7] stated that patients with post-acne scars and active acne had serum levels of survivin that were noticeably greater than the controls. Those with active acne, however, had greater levels of survivin than those with post-acne scars, the researchers discovered. They employed a different grading system to categorize the severity of the condition, which might account for the disparity (they used simple grading system whereas we used GAGS). This is in line with previous research that found that the keratinocytic proliferative and inflammatory phases, which are critical to the etiology of acne lesions [29, 30], are associated with an increase in survivin.

In line with our results, According to **El-Mokadem *et al.*** [31], the level of survivin was statistically significantly higher in the post-acne scars group than it was in the active acne and control groups (P 0.001). Moreover, there was a statistically significant rise in serum survivin levels as compared to the control group in patients with active acne (P 0.001). A statistically significant positive link was also seen between survivin level and the severity of the acne.

In recent research by **Kader and Akda** [32], acne sufferers exhibited serum survivin levels that were significantly greater (153.4 pg/ml) than the control group (104.2 pg/ml). Also, there was a substantial association between the SCAR-S score and survivin levels as well as a positive relationship between survivin and the severity of the acne. In a comparable research, **Sarac *et al.*** [33] discovered that acne vulgaris patients' serum levels of survivin were substantially (P 0.05) higher (153.44 pg/ml) than those of the control group (104.17 pg/ml). Also, there was a strong correlation between survivin levels and the SCAR-S score and acne stage.

Much research have shown some links with this problem, even if the actual source of the elevated survivin level in active acne cannot be determined [8, 29-30]. Survivin was also seen in inflammatory and keratinocyte proliferation, two processes that are essential for the development of acne lesions, in similar investigations [34]. As a result, we proposed that serum

survivin level be utilized as a new marker for the degree of post-acne scarring. Future research may also focus on survivin as a therapy for acne, particularly the severe kind that might impair a patient's quality of life.

In the present study, there was no significant difference in the polymorphism of survivin rs-9904341 genotype among the groups of the study ($P > 0.05$). Our results revealed that there is no significant difference in the different gene polymorphism (GG, CG and CC) between active acne patients and post-acne scars patients. Meanwhile, there is no significant association between the different polymorphisms of survivin rs-9904341 genotype and serum survivin levels of the studied groups.

Also, there was no significant difference in the distribution of survivin rs-1042489 genotype among the groups of the study ($P > 0.05$) for each. Our results revealed that there is no significant difference in the different gene polymorphisms (TT, TC and CC) between active acne patients and post-acne scars patients. Meanwhile, there is no significant association between the different polymorphisms of survivin rs-1042489 genotype and survivin levels in the serum.

Our results showed that there was no statistically significant difference in the genotype distribution of the rs-9904341 SNPs in patients with different grades of post-acne scars and patients with different grades of acne. Also, there is no statistically significant difference in the genotype distribution of the rs-1042489 SNPs in patients with different grades of post acne scars and patients with different grades of acne.

To the best of our knowledge, no research have previously examined the function of the survivin rs-1042489 genotype in relation to acne vulgaris. On the other hand, a single recent study found a strong correlation between Egyptian individuals' survivin rs9904341 genotypes and susceptibility to acne vulgaris [35]. However, further research is required to provide a clearer picture of the relationship between various survivin gene variants and acne vulgaris susceptibility and/or severity. This is because genetic polymorphism studies must be undertaken on a large population.

CONCLUSION

It could be concluded that survivin may be used as a diagnostic biomarker in acne vulgaris and as a prognostic tool for post acne scarring severity.

Survivin is involved in the pathogenesis of active acne vulgaris and more importantly, the pathogenesis of the development of fibrotic tissue in acne scars. No survivin polymorphism are found in Egyptian population.

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