

## Serum Level of Podoplanin in Patients with Acne Scars

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### Abstract

Skin inflammation vulgaris is a fiery procedure confined to the pilosebaceous units of the face, chest, upper arms, and back Podoplanin is a little film glycoprotein with an enormous number of O-glycoside chains and in this manner it has a place with mucin-type proteins. The point of this investigation was to uncover podoplanin job in the pathogenesis of skin break out scars. case control study included 30 patients experiencing scarring skin inflammation vulgaris and 30 patients experiencing non-scarring skin break out vulgaris moreover, 20 clearly solid people of coordinated age and sex as a benchmark group. Conclusion of AV was made based on the patient's history and the run of the mill clinical highlights. The all out seriousness score was gotten from the worldwide skin break out evaluating framework (GAGS). The serum activin-A levels estimated by catalyst connected immunosorbent examine (ELISA) We found that all out skin break out Vulgaris bunch indicated essentially higher serum Podoplanin when contrasted with control bunch scarring subgroups demonstrated altogether higher serum Podoplanin when contrasted with non-scarring subgroup . No critical contrasts were found in serum Podoplanin fixation as per sexual orientation and other hazard factors in skin inflammation vulgaris gathering. (P esteem >.0.5). Higher BMI, positive family ancestry, smoking, higher recurrence of abundance sun presentation, expending high caloric eating regimen, overabundance stress, higher serum Podoplanin level were related with danger of Acne Vulgaris scarring in univariable examination. In any case, facing huge challenge factors into multivariable investigation uncovered that positive family ancestry and higher serum Podoplanin were considered as independent indicators for Acne Vulgaris scarring.

### 1. Introduction

Skin inflammation vulgaris is a incendiary methodology confined of the pilosebaceous units of the face, chest, upper arms, What's more once again [1]. The presumed pathophysiology includes modification for keratinization inside the pilosebaceous unit bringing about comedone formation, expanded sebum production, burgeoning for Propionibacterium acnes (P. Acnes), and preparation of perifollicular aggravation [2].

Those initial preclinical aggravation to skin break out persists for the skin break out lesion's life cycle, from micro-comedones with shut comedones on incendiary lesions and inevitably to post-inflammatory erythema (PIE), post-inflammatory hyperpigmentation (PIH), Also scarring [3].

Skin break out influences those face clinched alongside An larger part for cases, with a number patients encountering a portion level about scarring, the seriousness of which correlates to skin break out review. Skin break out scars effect from a modified wound recuperating light of cutaneous inflammation, with incendiary cell infiltrates found clinched alongside 77 percent for atrophic scars [4].

Aberrant handling Furthermore debasement of collagen Throughout those recuperating procedure prompts different sorts for skin break out scars. Clinched alongside 80 will 90 percent of cases, there may be a net decimation for collagen in the dermis that brings about atrophic scars. Lesquerella commonly, there will be a net addition of collagen that brings about hypertrophic alternately keloid scars [5].

Podoplanin will be a little film glycoprotein for an extensive number of O-glycoside chains What's more In it belongs should mucin-type proteins. It could be found on the surface from claiming Numerous sorts from claiming typical units starting from Different germ layers. It will be available essential on the endothelium

of lymphatic vessels, kind i pneumocytes and glomerular podocytes. Expanded levels of podoplanin alternately its neo-expression need been found over various sorts for mankind's carcinomas. This little sialomucin is likewise seen on the surface of cancer-associated fibroblasts (CAFs) [6].

Tissue damage reasons those interruption of blood vessels What's more extravasation of blood constituents. Those blood cluster re-establishes hemostasis Also gives An temporary extracellular grid to cell movement. Platelets not main encourage the framing of a hemostatic plug as well as emit a few mediators for wound healing, for example, such that platelet-derived Growth factor, that Lure Furthermore initiate macrophages Furthermore fibroblasts. It might have been shown that platelets down-regulated podoplanin function, which prompted An decrease in keratinocyte motility [6]. Those point from claiming this ponder might have been should uncover podoplanin part in the pathogenesis about skin break out scars.

### 2. Patient and method

The study was conducted as a case control study. The study included 30 patients suffering from scarring acne vulgaris and 30 patients suffering from non-scarring acne vulgaris in addition, 20 apparently healthy individuals of matched age and sex as a control group. All patients were selected from the Outpatient Clinic of Dermatology and Andrology Department in Benha University Hospitals in period from October 2018 to October 2019.

**Inclusion criteria** was Patients with scarring acne vulgaris, Patients with non-scarring acne vulgaris, Age between 12 and 30 years old.

**Exclusion criteria** was Patients with history of active infection, inflammatory and autoimmune local and systemic diseases such as asthma, rheumatoid arthritis and acute ischemia, Patients with malignant disorders

such as leukaemia, lymphoma and prostatic cancer, Pregnancy and lactation and Patients with liver or kidney diseases.

- Detailed dermatological examination to evaluate clinical variant, severity of AV and presence of acne scars and their types.
- Diagnosis of AV was made on the basis of the patient's history and the typical clinical features of non-inflammatory lesions form, including closed (whiteheads) and open (blackheads) comedones, and inflammatory lesions including papules, pustules, nodules and/or cysts on the face, chest and upper back.
- The total severity score was derived from the global acne grading system (GAGS) in which the intensity and the distribution of pilosebaceous units are evaluated for the six locations (face/forehead, left and right cheeks, nose, chin, and chest and upper back) as 0 (no lesions), 1 (one comedone), 2 (one papule), 3 (one pustule), or 4 (one nodule), with each of those ratings multiplied by a factor specific for that location. The global score is the sum of all the local scores. Acne is evaluated as: no acne (0 points), mild (1–18), moderate (19–30), severe (31–38) or very severe (> 39) Tabel (1) .

Five milliliters from claiming venous blood might have been gathered from every subjects ahead plain tubes. The tubes were permitted on cluster and centrifuged instantly toward 3000 rpm to 15 min with uproot those serum. Those serum tests were divided Furthermore kept during -20 °C until utilize. The serum activin-A levels measured by catalyst interfaced immunosorbent test (ELISA) unit to investigate utilize best (catalogue number: 201-12-0124, sun red Bio, China).

The unit utilization An double-antibody sandwich enzyme-linked immunosorbent test (ELISA) will test the level about mankind's Podoplanin (PDPN) done tests. Podoplanin (PDPN) might have been included will monoclonal immune response catalyst great which is pre-coated with mankind's Podoplanin (PDPN) monoclonal antibody, incubation; then, Podoplanin (PDPN) antibodies marked for biotin might have been added, Also joined with Streptavidin-HRP to structure resistant complex; afterward brooding and washing once more might have been conveyed out to uproot those uncombined catalyst. After that chromogen result A, B, might have been included the shade of the fluid progressions under the blue, Furthermore toward the impact about acid, the shade At last got to be yellow. The chroma about shade and the focus of the human substance Podoplanin (PDPN) of example were emphatically corresponded.

### 2.1 Inject samples

- 1- Blank well: Chromogen solution A and B, and stop solution were added; other operations are the same.
- 2- Standard wells: standard 50µl, Streptavidin-HRP 50µl were added.

- 3- To be test wells: sample 40µl, and both PDPN – antibody 10µl and Streptavidin-HRP 50µl were added. Then the sealing memberance was sealed, and gently shacked, incubated 60 minutes at 37°C.
- 4- Confection: 30 times the 30×washing concentrate was diluted with distilled water as standby.
- 5- Washing: the memberance carefully was removed, and the liquid drained, the remaining water was shacked away.
- 6- Chromogen solution A 50µl was added, then chromogen solution B 50µl to each well. Gently mixed, incubated for 10 min at 37°C away from light.
- 7- Stop: Stop Solution 50µl was added into each well to stop the reaction (the blue changes into yellow immediately).
- 8- Final measurement: blank well was taken as zero, the optical densit (OD) measured under 450 nm wavelength which was carried out within 15min after adding the stop solution.

The standard density was taken as the horizontal, the OD value for the vertical, the standard curve was drawn on graph paper, the corresponding density was finded according to the sample OD value by the Sample curve (the result was the sample density) or the straight line regression equation of the standard curve was calculated with the standard density and the OD value, with the sample OD value in the equation, the sample density calculated.

### 3. Results

The mean age of Acne Vulgaris patients was 20.8 years. Male patients represented 16.7%, while females represented 83.3%. In addition to 20 healthy control subjects of matched age and gender.

Mean age of non-scarring cases was 19.9 years. They were 20% males and 80% females. Mean age of scarring cases was 21.7 years. They were 13.3% males, 86.7% females. No significant differences were found in age and gender between scarring and non-scarring cases ( $p > 0.05$  for each).

No significant differences were found in BMI between acne vulgaris and control. As well as between scarring and non-scarring cases.

Positive family history, smoking, excess sun exposure, hyperglycemic diet and psychological stress were significantly associated with acne vulgaris when compared to control group, as well as when comparing scarring to non-scarring cases. ( $P$  value 0.012 , 0.005 , 0.024 , 0.015 , 0.032 , 0.640 )

However, no significant differences were found in systemic diseases between all studied groups and subgroups.

Face was affected in all studied patients , chest in 1 case. While back was affected by non-scarring acne, with significant difference versus scarring group  $p = 0.005$ ). Onset, course, duration, severity, and previous treatment did not differ significantly between scarring and non-scarring acne groups. ( $P$  value  $> 0.05$  each) as shown in table .

Total acne Vulgaris group showed significantly higher serum Podoplanin when compared to control group (median=39, 82.9 respectively; p=0.020). In addition, scarring subgroups showed significantly higher serum Podoplanin when compared to non-scarring subgroup (median=68.4, 271.9 respectively, p<0.001).

Receiver operating characteristic (ROC) curve of serum Podoplanin was conducted for discrimination between acne vulgaris cases and control groups. Serum Podoplanin showed good AUC (AUC=0.874). At cut off value of 57.7, sensitivity was 80%, specificity was 85%, PPV was 94.1%, NPV was 58.6%, accuracy was 81.3%.

**3.1 predictive value**

Roc bend from claiming serum Podoplanin might have been directed for separation between scarring Also non-scarring skin inflammation vulgaris situations. Serum Podoplanin demonstrated great auc (AUC=0. 854). In cut off worth of 74. 35, affectability might have been 90%, specificity might have been 70%, PPV might have been 75%, same way as the NPV might have been 87. 5%, exactness might have been 80%.

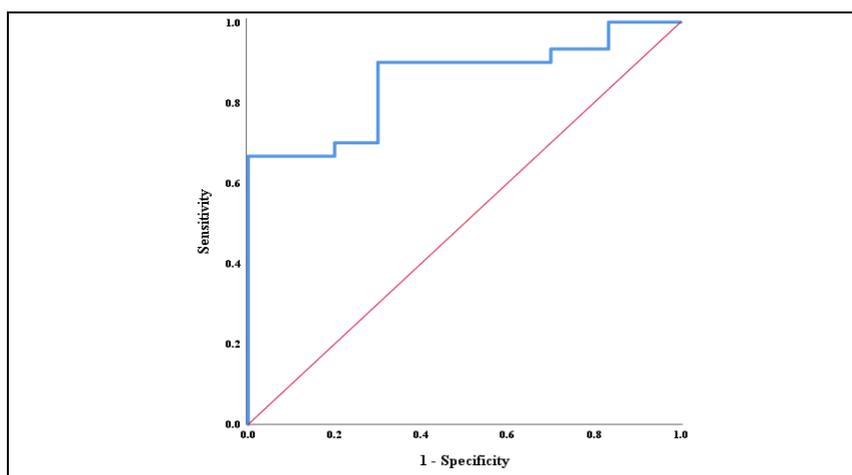
No critical contrasts were discovered in serum Podoplanin centralization as stated by sexual orientation Furthermore other danger figures in skin inflammation vulgaris aggregation. (P esteem >. 0. 5). Serum Podoplanin fixation expanded for expanded seriousness. Serum Podoplanin focus didn't vary as stated by onset Also course.

Serum Podoplanin demonstrated critical certain correspondence for seriousness Also scarring. No noteworthy correlations were found between serum Podoplanin for age, BMI Furthermore span Previously, skin inflammation vulgaris assembly.

Logistic relapse investigation might have been led to prediction for skin inflammation vulgaris development, utilizing age, gender, BMI, smoking, FH, hazard factors, serum Podoplanin Similarly as covariates. Certain FH, smoking, higher recurrence sun exposure, secondary caloric diet, abundance stress, higher serum Podoplanin level were connected with danger from claiming skin inflammation vulgaris event for univariable dissection. However, taking noteworthy danger figures under multivariable examination uncovered that just higher serum Podoplanin might have been recognized Concerning illustration a predictor to skin inflammation vulgaris advancement.

Ordinal relapse investigation might have been directed for prediction from claiming skin break out severity, utilizing age, gender, BMI, smoking, FH, danger factors, onset, course, duration, serum Podoplanin Likewise covariates. Progressive course and higher serum Podoplanin level were viewed as predictors for a greater amount extreme skin inflammation vulgaris for uni Also multivariable analyses.

Logistic relapse investigation might have been directed for prediction about skin inflammation vulgaris scarring, utilizing age, gender, BMI, smoking, FH, hazard factors, onset, course, duration, serum Podoplanin Concerning illustration covariates. Higher BMI, sure gang history, smoking, higher recurrence about overabundance sun exposure, devouring helter skelter caloric diet, abundance stress, higher serum Podoplanin level were connected with danger of skin inflammation vulgaris scarring for univariable Investigation. However, taking critical danger figures under multivariable dissection uncovered that sure family history and higher serum Podoplanin were viewed as Likewise independant predictors for skin inflammation vulgaris scarring.



**Fig (1)** ROC curve of serum Podoplanin for discrimination between scarring and non scarring Acne Vulgaris cases.

**Table (1)** Comparison of serum Podoplanin concentration according to gender and risk factors in acne vulgaris group.

		N	Podoplanin concentration (ng/mL)					P
			mean	SD	median	minimum	maximum	
<b>Gender</b>	Male	10	451.5	784.8	55.4	41.7	2046.9	0.184
	Female	50	247.7	337.2	87.5	41.2	1609.6	
<b>family history</b>	Negative	41	250.5	430.5	68.4	41.2	2046.9	0.425
	Positive	19	349.1	466.7	93.5	47.7	1814.7	
<b>Smoking</b>	No	42	200.4	339.3	168.6	41.2	1814.7	0.128
	Yes	18	371.4	584.9	248.3	41.7	2046.9	
<b>sun exposure</b>	Less	42	284.6	486.9	61.1	41.2	2046.9	0.939
	Excess	18	274.9	320	119.9	48.7	1257.6	
<b>fat diet</b>	low	39	246.2	436.5	68.1	41.2	2046.9	0.400
	High	21	347.7	451.7	109.4	49.2	1814.7	
<b>stress</b>	Less	38	227	389.8	60.1	41.2	1814.7	0.209
	Excess	22	376.2	513.2	114.4	43.2	2046.9	

SD, standard deviation.

**Table (2)** Comparison of serum Podoplanin concentration according to clinical data in acne vulgaris group.

		N	Podoplanin concentration (ng/mL)					P
			mean	SD	median	minimum	maximum	
<b>Onset</b>	Gradual	29	228.3	322.2	72.1	41.2	1257.6	0.368
	Sudden	31	331.7	529	109.4	49.2	2046.9	
<b>Course</b>	Stationary	23	180.7	348	59.7	41.2	1609.6	0.163
	progressive	37	344.5	483.5	119.9	48.7	2046.9	
<b>Severity</b>	Mild	24	66.8	34.6	57.7	41.2	210.9	<0.001
	moderate	25	269.9	222.9	248.3	61.1	779.4	
	Severe	11	777.4	801.7	149.5	83.8	2046.9	

SD, standard deviation.

**Table (3)** Correlations of serum Podoplanin with other studied parameters in acne vulgaris group.

	Podoplanin	
	r	P
<b>Age</b>	0.273	0.103
<b>BMI</b>	0.206	0.118
<b>Duration</b>	0.060	0.651

r, Spearman's correlation coefficient.

**Table (4)** Regression analysis for prediction of Acne Vulgaris development.

	Univariable				Multivariable			
	P	OR	95% CI		P	OR	95% CI	
<b>Age</b>	0.109	0.907	0.806	1.022				
<b>Gender</b>	0.861	0.882	0.217	3.588				
<b>BMI</b>	0.963	0.995	0.819	1.210				
<b>Positive family history</b>	0.020	3.215	1.203	8.595	0.200	2.822	0.578	13.775
<b>Smoking</b>	0.026	3.090	1.147	8.322	0.088	3.387	0.835	13.737
<b>Excess sun exposure</b>	0.026	3.090	1.147	8.322	0.667	1.383	0.316	6.062
<b>high fat diet</b>	0.032	2.411	1.081	5.382	0.260	2.016	0.595	6.835
<b>Excess stress</b>	0.009	3.600	1.372	9.446	0.119	2.897	0.759	11.048
<b>Podoplanin</b>	0.001	1.031	1.013	1.050	0.005	1.029	1.008	1.049

OR, odds ratio; CI, confidence interval.

**Table (5)** Regression analysis for prediction of severity within Acne Vulgaris patients.

	Univariable				Multivariable			
	P	OR	95% CI		P	OR	95% CI	
Age	0.129	1.052	0.985	1.124				
Gender	0.151	1.828	0.803	4.161				
BMI	0.344	1.053	0.946	1.172				
Positive family history	0.468	0.796	0.429	1.475				
Smoking	0.976	0.990	0.533	1.840				
Excess sun exposure	0.261	1.425	0.769	2.642				
high fat diet	0.577	1.185	0.653	2.151				
Excess stress	0.523	1.212	0.672	2.185				
Acute onset	0.196	1.460	0.823	2.590				
Progressive course	<0.001	5.011	2.502	10.036	<0.001	5.737	2.601	12.654
Longer duration	0.471	1.049	0.921	1.194				
Podoplanin	<0.001	1.002	1.001	1.004	<0.001	1.005	1.001	1.012

OR, odds ratio; CI, confidence interval.

**Table (6)** Regression analysis for prediction of scarring within Acne Vulgaris patients.

	Univariable				Multivariable			
	P	OR	95% CI		P	OR	95% CI	
Age	0.113	1.061	0.986	1.141				
Gender	0.489	1.355	0.574	3.199				
BMI	0.004	1.258	1.076	1.47	0.039	1.678	1.028	2.740
Positive family history	0.013	2.49	1.211	5.119	0.071	2.108	0.846	9.747
Smoking	0.005	2.909	1.372	6.166	0.056	1.858	0.947	10.600
Excess sun exposure	0.025	2.294	1.11	4.744	0.060	1.594	0.935	2.563
high fat diet	0.015	2.362	1.179	4.731	0.467	1.674	0.418	6.715
Excess stress	0.033	2.095	1.063	4.131	0.665	1.459	0.264	8.079
Acute onset	0.438	1.286	0.681	2.43				
Progressive course	0.426	1.305	0.678	2.511				
Longer duration	0.556	1.045	0.903	1.208				
Podoplanin	0.002	1.012	1.004	1.02	0.023	1.022	1.003	1.042

OR, odds ratio; CI, confidence interval.

#### 4. Discussion

Skin break out will be An unending ailment predominantly influencing junior grown-ups from regarding those agdistis of 11 years, peaking around 16 years, for hold on in done A percentage of the 20s Also 30s. It will be connected with noteworthy psycho-social burden, including depression, anxiety, deficits On personal satisfaction for life Concerning illustration extraordinary Similarly as patients with incessant incapacitating asthma, epilepsy, diabetes, alternately joint inflammation [7].

Skin break out will be frequently connected with the improvemen about scars, principally On direct alternately extreme incendiary types as well as clinched alongside exactly gentle types also [8]. In patients for direct acne, scars could type from papules (inflammatory lesions) alternately post-inflammatory lesions with just a third determining inside six months, Subsequently those join the middle of initial skin break out oversaw economy Also scar counteractive action. In spite of it need been poorly researched, skin break out scarring will be frequently connected for oppressive psycho-social

results Furthermore deficits clinched alongside personal satisfaction about term [9].

Counteractive action remains an essential methodology for skin break out scarring. Thus, it is paramount with figure out which patients need aid toward expanded danger for scarring thereabouts that they might a chance to be identifier for An objective from claiming instituting viable skin break out treatment [10].

This situation control study might have been directed should assess serum level for Podoplanin over 30 patients with scarring Furthermore 30 patients for non-scarring skin inflammation vulgaris. To addition, 20 clearly solid people of matched period and sex as a control gathering.

At patients were subjected will complete history, finish all examination including, dermatological clinical examination Furthermore estimation about serum level podoplanin Previously, patients Furthermore control bunches Toward catalyst interfaced immunosorbent test (ELISA).

In this study, there might have been a hugeness Contrast between skin break out evaluating and the event about scars (p worth >0. 05). As those non-scarring bunch required just gentle (13 patients) , moderate (11 patients) skin break out Also separate (6 patients) same time those scarring assembly needed main extreme (30 patients) skin break out.

This discovering backs those past outcomes about holland et al. [11], they demonstrated a solid relationship between seriousness for aggravation connected skin break out and the improvemen about scarring, suggesting that treating early aggravation in skin break out lesions might be the best approach with forestall skin break out scarring.

Nonetheless Fabbrocini et al. [12] news person A percentage level from claiming scarring in up to 87% of patients with gentle to moderate skin break out. This might make due to delay looking for medicine.

Clinched alongside addition, Ghodsi et al. [13] discovered that patients anguish from extreme incendiary skin break out were 3. 4 with 6. 8 times less averse on create scars contrasted with the individuals for lesquerella extreme skin break out.

Of the best about our knowledge, this will be the main ponder on assess serum level for Podoplanin Previously, skin break out Furthermore will explore its part in the pathogenesis from claiming skin break out scars. Those mean quality for serum podoplanin might have been significsntly higher to patients for scarring av over both non scarring Furthermore control Assemblies (P. Value= 0. 05).

We discovered that downright skin inflammation vulgaris gathering indicated essentially higher serum Podoplanin when contrasted with control assembly (median=39, 82. 9 respectively; p=0. 020). In addition, scarring subgroups indicated essentially higher serum Podoplanin At contrasted with non scarring subgroup (median=68. 4, 271. 9 respectively, p<0. 001).

Podoplanin is a little cell-surface mucin-like glycoprotein that assumes a urgent part in the improvement of the alveoli, heart, Furthermore lymphatic vascular framework. Rising confirmation demonstrates that it is Additionally included in the control from claiming mammary stem-cell action What's more biogenesis about platelets in the bone marrow, What's more exerts a paramount capacity in the safe reaction. Podoplanin outflow may be upregulated in distinctive Mobile types, including fibroblasts, macrophages, t aide cells, What's more epithelial cells, Throughout aggravation Furthermore cancer, the place it assumes imperative parts.

Podoplanin will be embroiled in constant incendiary diseases, for example, such that psoriasis, numerous sclerosis, What's more rheumatoid arthritis, advertises inflammation-driven and cancer-associated thrombosis, and fortifies growth borealis Attack Also metastasis through an assortment about methodologies. To fulfill its living functions, podoplanin must cooperate for other proteins found in the same Mobile or over neighbor phones. Those tying for podoplanin should its ligands

prompts regulation for indicating pathways that control proliferation, contractility, migration, epithelial–mesenchymal transition, What's more remodeling of the extracellular grid.

No noteworthy contrasts were discovered clinched alongside serum Podoplanin fixation as stated by sexual orientation What's more different danger figures in skin inflammation vulgaris aggregation. (P quality >. 0. 5). Serum Podoplanin centralization expanded for expanded seriousness. Serum Podoplanin centralization didn't contrast as stated by onset and course.

Serum Podoplanin indicated noteworthy certain relationship with seriousness and scarring. No noteworthy correlations were found the middle of serum Podoplanin with age, BMI What's more span clinched alongside skin inflammation vulgaris assembly.

Higher serum Podoplanin level were connected with hazard of skin inflammation vulgaris event for univariable Investigation. However, taking critical danger figures under multivariable dissection uncovered that best higher serum Podoplanin might have been acknowledged Likewise An predictor to skin inflammation vulgaris improvemen.

Higher serum Podoplanin level were connected with hazard of skin inflammation vulgaris scarring over univariable examination. However, bringing critical danger figures under multivariable dissection uncovered that sure family history and higher serum Podoplanin were acknowledged Concerning illustration independant predictors to skin inflammation vulgaris scarring.

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