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ORIGINAL ARTICLE

Assessment Of Serum Angiopoietin-2 Level In Patients With Psoriasis Vulgaris

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ABSTRACT

Background: Psoriasis is a chronic inflammatory immune-mediated hyperproliferative skin disease. Angiogenesis has an important role in the pathogenesis of psoriasis, occurring even before plaque formation. Angiopoietins have an important role in angiogenesis so described as angiogenic factors, this study aimed to evaluate Angiopoietin-2 serum level in psoriasis Vulgaris patients and to evaluate if there is a relation between serum Angiopoietin-2 level and the disease activity.

Patients and Methods: This is a case-control study that included 40participants, 20 are patients and other 20 are healthy subjects. Complete general, family, past history was documented, the dermatological examination was done to all patients included in the study. The study was approved by the research ethical committee of Faculty of Medicine Zagazig University.The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Results: There is a highly statistically significant difference between the studied groups regarding serum angiopoietin 2 level, higher in the psoriasis group. In the psoriasis group, there is a significant positive correlation between angiopoietin 2 serum level and psoriasis area severity index. There is a statistically significant difference in serum angiopoietin 2 level and disease course, higher in progressive type.

Conclusions: Angiopoietin 2 is closely associated with the evolving of microvascular proliferation in psoriasis and its level increase with the severity of the disease. Based on our results, we suggest that serum Ang2 level act as a possible useful biomarker of Psoriasis Vulgaris.

Also, the major role of Ang2 in systemic pathological processes in psoriasis.

Keywords: Angiopoietin-2, psoriasis, Angiogenesis

INTRODUCTION

Psoriasis is a chronic relapsing inflammatory hyperproliferative immune-mediated skin disease. Presented by patches of abnormal skin, these skin patches are typically red, itchy, and scaly. It affects about 1-3% of the world population.[1] with an equal sex distribution and may manifest itself at any age, with severe impact on the quality of the patient life.[2] Although psoriasis is one of the most studied dermatological diseases, the pathogenesis of the disease is still not completely clarified. The first events in psoriasis are epidermal or dermal are not completely understood.[3 Angiogenesis seems to have a principal role in the psoriasis phenotype. The expansion of the vascular network in skin cells is mediated by the secretion of many pro-angiogenic growth factors. Also, pro-inflammatory cytokines participate in this process by activating endothelial cells and exerting pro-angiogenic action. It is now well known that keratinocytes in lesional skin are a significant source of pro-angiogenic cytokines in psoriasis.[4] The dermal microvascular dilatation and expansion associated with abnormal orientation and dilatation of capillaries in the psoriatic skin biopsies, suggest that the disease is dependent on angiogenesis. Angiopoietins known as a major ligands of the endothelial-specific receptor Tie2. Ang 1stimulate Tie2 signaling as a receptor activator and maintains blood vessel

formation, Ang 2 destabilizes vessels through blocking Tie2 signaling as an antagonist of Ang 1and acts with VEGF to initiate angiogenesis.[5] High Ang-2 levels lead to weaken and impaired integrity of the endothelium ,enhance monocyte adhesion and migration by sensitizing endothelial cells to tumor necrosis factor-α (TNF-α).[6] Psoriasis treatment is accompanied by decrease in the Angiopoietin-2 level. Levels of Angiopoietin-1 and Tie2 are also decreased by psoriatic treatment, but not markedly as Angiopoietin-2, from these expression profiles, Angiopoietin-2 plays principle role in the vascularization of the psoriatic plaque. [7]

AIM OF THE STUDY:

Was to evaluate Angiopoietin-2 serum level in patients with psoriasis vulgaris and to evaluate if there is a possible relation between serum Angiopoietin-2 level and the disease activity

PATIENTS AND METHODS

After obtaining approval from Research Ethics Committee of Zagazig Universityy. This case-control study was carried out in outpatient Clinic of Dermatology, Venereology and Andrology Department, Faculty of Medicine, Zagazig University from January 2018 to November 2018. This study included 40 participants, 20 are patients and other 20 are healthy subjects. Written informed consent was obtained from each participant before the beginning of this study. The participants were classified into two groups Group I (patients group): include twenty patients with psoriasis Vulgaris. They include 7 male (35%) and 13 female(65%). Group II (control group): include twenty healthy individuals matched in age and gender. Exclusion criteria include previous systemic medical or phototherapy for psoriasis for at least one month ago, Patients using any immunosuppressant during last 3 months, Pregnant and lactating females.

Complete medical history was documented, General and dermatological examination was done to all patients participate in the study, Severity of psoriasis vulgaris is determined by psoriasis area severity index, PASI score. PASI is the most used measurement tool for psoriasis. It is assess the lesions severity, area affected and summing these two factors into one score from 0, no disease to72, maximum disease. Specimen collection, 3ml of venous blood were collected by vein puncture under complete aseptic condition from every subject then put in a sterile, dry, clean separator gel tube for serum isolation and left to clot. After clotting, the samples were centrifuged about 20 minutes at 2000-3000 rpm. Separation and storage of serum immediately at -20°C in blood bank, Angiopoietin-2 was measured in serum sample using Human Angiopoietin-2, ANGPT2 ELISA kit, Chongqing Biospes, China.

STATISTICAL ANALYSIS

Software SPSS(Statistical Package for the Social Sciences) version 20 was used for performing data analysis. Quantitative variables were described by using standard deviations and their means. Categorical variables were presented through their absolute frequencies and chi square test used to compare the proportion of categorical data. To determine variables independently associated with serum angiopoietin level we use linear stepwise regression analysis. Statistical significance level was set at 5% ($P<0.05$). If $p\leq0.001$there is highly significant difference.

RESULTS

The demographic features of the studied groups were analyzed and show statistically non-significant differences between both groups regarding age or gender as shown in **table(1).** The largest percentage of patients had progressive course, negative family history, and had lesions on trunk, upper and lower extremities as shown in **Table (2).** The mean Psoriasis area severity index was 20.59 (±10.54). mean age of onset was 19.43 (± 13.5) and the disease duration ranged from 8.1 to 38.1 years old. largest percentage received combined topical steroid and phototherapy. **Table(3)** shows a highly significant statistical difference between the studied groups regarding serum angiopoietin 2 level, higher in the psoriasis group. In the psoriasis group, there is a significant positive correlation between serum Angiopoietin-2 level and psoriasis area severity index. In the control group, there is a non-significant negative correlation between serum Angiopoietin-2 level and age as shown in **table (4).** The statistically non-significant difference in serum angiopoietin 2 level and family history is shown in **table(5). Table(6)** shows a statistically significant difference in serum angiopoietin 2 level and lesion site with patients whose lesions on (head, trunk, upper and lower extremities) had the highest angiopoietin 2 level and statistically significant difference in serum angiopoietin 2 level and disease course, higher in progressive type.

Table (1) : demographic characteristics of studied groups

	Psoriasis group	Control group	Test	p
Age: mean ± SD	26 ± 14.79	26 ± 14.79	Z (0)	1

	Psoriasis group	Control group	Test	p
range	6 – 62	6 - 62		(NS)
Gender: **Male** **Female**	 7 (35) 13 (65)	 7 (35) 13 (65)	X^2 (0)	 1 (NS)

Table (2): Clinical data of the psoriasis cases group

	N (%)
Course: **Stationary** **Progressive**	 4 (20) 16 (80)
Family history: **Negative** **Positive**	 19 (95) 1 (5)
Site: **Head, trunk, lower extremities** **Upper and Lower extremities** **Trunk, UL, LL** **all** **Trunk, UL** **Head,Upper and Lower extremities** **head, UL, LL** **Trunk**	 1 (5) 3 (15) 6 (30) 2 (10) 3 (15) 2 (10) 1 (5) 2 (10)
Age of onset (year): **mean ± SD** **Range**	 19.43 ± 13.5 3 - 60
Duration (year): **mean ± SD** **Range**	 6.68 ± 5.88 0.5 - 24
Psoriasis area severity index:	
mean ± SD **Range**	20.59 ± 10.54 8.1 – 38.1

Table (3): Serum Angiopoietin-2 levels in studied groups

	Psoriasis group	Control group	MW	P
Serum Angiopoietin-2: **mean ± SD** **Range**	 28.904 ± 33.806 5.088- 147.974	 6.495 ± 1.933 3.397 – 9.136	-4.058	<0.001 (HS)

Table (4): correlation between clinical data(age, Duration, Age of onset ,Psoriasis area severity index)

	Psoriasis group		Control group	
	R	P	R	p
Age	0.154	0.516	-0.034	0.886
Duration	0.233	0.324		
Age of onset	-0.02	0.932		
Psoriasis area severity index	0.657	0.002		

p<0.05 is statistically significant

Table (5): relation between disease course, family history of studied cases and serum Angiopiotein 2

	Serum angiopoietn 2 level		
	Mean ± SD	MW	p
Course: **Stationary** **Progressive**	 6.18 ± 1.02 34.58 ± 35.71	 -2.835∞	 0.005 (S)
	Mean ± SD	test	p
Family history: **Negative** **Positive**	 26.75 ± 33.3 69.8 ± 0	 -1.474	 0.140 (NS)

Table (6): relation between site of lesion in studied cases and serum Angiopiotein 2:

	Serum angiopoietn 2 level		
	Mean ± SD	KW	P
Trunk **Head.Trunk, lower extremities** **Upper and Lower extremities** **trunk, UL, LL** **all** **trunk, UL** **Head.Upper and Lower extremities**	6.13 ± 0.83 29.29 ±7.04 11.65 ±6.78 51.93 ± 50.98 53.45 ± 23.12 12.22 ± 5.58 8.58 ± 2.14	13.49	0.036 (S)

Table (7): linear stepwise regression analysis showing variables independently associated with serum angiopoietin 2 level

	Unstandardized Coefficient		Standardized Coefficients	t	p
	Beta	Standard error	Beta		
psoriasis area severity index	1.502	0.668	0.468	2.248	0.037*

DISCUSSION

The current study was conducted to estimate serum Angiopoietin-2 level in psoriasis Vulgaris patients, to compare its level with a healthy control group, and to detect if there is a correlation between Angiopoietin-2 level and disease activity. Firstly, the two groups show no statistically significant difference as regard patients' characteristics (age, sex). These findings run in agreement with.[8] reported that Psoriasis affects both sexes equally. [9] reported that Psoriasis commonly appears for the initial time between ages of 15to 25 years. In our study mean age of studied patients within the psoriasis group was 26 years old (SD 14.79). In our study, the largest majority of study participants had a negative family history. This results in disagrees with [10]. [11] demonstrated that affected parent's history, 44% in type I, 0% in type II. The present study demonstrated that there is a highly significant statistical difference between the studied groups regarding serum level of angiopoietin 2, higher in psoriasis patients than in healthy controls. Our results were in agreement with the results reported.[12] found that serum levels of Ang2 were significantly higher in psoriasis patients than in healthy controls, P = 0.032. [12] found that there is a positive significant correlation between serum level of angiopoietin 2 and psoriasis area severity index score in psoriasis group. The findings run in agreement with the result of our study. In a northeastern Han Chinese population, there is an association between ANGPT2 polymorphisms and increased risk of PV. [13] Processes of inflammation and Angiogenesis are highly interlinked. [6] Ang-2 consider an important regulator of angiogenesis and influences inflammation. [14] Ang-2 is able to sensitize endothelial cells to many inflammatory signals as TNF-a so leads to up-regulation of related adhesion molecules, facilitating leukocyte adhesion, chemotaxis, and having a role in inflammatory responses during psoriasis development. This suggests that a dysregulated Ang system contributes to systemic events in the psoriatic patient such as cardiovascular disease [6].[15] reported that coronary heart disease patients undergo cardiovascular complications in a frequent manner after doing PCI.[16] reported that which explains the occurrence of cardiovascular events of post-PCI in a short period is that high Ang-2 levels.

[17] They found that Ang-2 levels are raised in patients with sepsis.

CONCLUSION

It could be concluded from this study that Angiopoietin 2 is linked to a large extent with the proliferation of microvascular network in psoriasis, its level increases with disease severity, and serum Ang-2 level act as a possible benefit biomarker of and has an important role in the occurrence of the systemic pathological processes in psoriasis Vulgaris

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