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Original Research Article

Neovascularization in Psoriatic Patients

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Abstract

Although angiogenesis may not be the main event in the pathogenesis of psoriasis, identifyingthe pathways leading to angio-proliferation mayaid in discovery of novel antipsoriatic drugs. Vascular endothelial growth factor is a principal regulator of physiological and pathologicalneoangiogenesis.
The aim of the study is to assess the serum level of vascular endothelial growth factor in psoriatic patients and its correlation with Psoriasis area and severity index score (PASI score).
One hundred consentingpsoriatic patients(males and females)aged 20-60 years who attended different medical centers including Al-Sadr Medical City and department of laser research in AL-Najaf city and Marjan Medical City in AL-Hilla-Iraq.Psoriasis area and severity index assessment was done for each patient. Blood samples were collected for vascular endothelial growth factor measurement**.**
The serum level of vascular endothelial growth factor was significantly increased in all groups of,psoriatic,patients comparedto healthy controls as well as serum vascular endothelial growth factor showed positive correlation with PASI score.

Keywords: Serum vascular endothelial growth, Psoriasis area and severity index, Psoriasis.
List of abbreviation:sVEGF=serum vascular endothelial growth,PASI=Psoriasis area and severity index, SD=standard deviation ,r=correlation coefficient, PsA=psoriatic arthritis**.** ELISA= Enzyme Linked Immuno Linked Sorbant Assay.

عملية تكوين اوعية دموية جديدة لدى مرضى الصدفية

الخلاصة

بالرغم ان تكوين اوعية دموية جديدة هي ليست الحدث الرئيسي في نشوء مرض الصدفية ولكن معرفة الطريق الذي يؤدي الى نشوء الاوعية الدموية سوف يؤدي الى اكتشاف علاج جديد لمرضى الصدفية.ان عامل النمو البطاني الوعائي هو المنظم الرئيسي في عملية تكوين اوعية دموية جديدة سواء كانت فسلجية او مرضية .هدف الدراسة هو لقياس مستوى عامل النمو البطاني الوعائي في مصل مرضى الصدفية ومقارنتها مع السيطرة وكذلك معرفة علاقة عامل النمو البطاني الوعائي و مؤشر المساحة والشدة للصدفية.

تضمنت الدراسة ١٠٠ مريض من مرضىالصدفية المراجعين لمركز بحوث الليزر في كلية الطب جامعة الكوفة واستشارية الجلدية في مستشفى الصدر في النجف الاشرف ومرضى استشارية الجلدية في مستشفى مرجان في بابل .خضع كل مريض في هذه الدراسة لتفاصيل التاريخ الطبي والفحص البدني. وقد تم تقييم مؤشر المساحة والشدة للصدفية .ايضا تم جمع عينة الدم لأجراء الاختبارات البيوكيميائيةلقياس عامل النمو البطاني الوعائي.كانت قيم عامل النمو البطاني الوعائي في مصل مرضى الصدفية عالية جدا قياسا بالسيطرةوكذلك يوجد ارتباط ايجابي بين عامل النمو البطاني الوعائي و مؤشر المساحة والشدة للصدفية.

مفاتيح الكلمات: عامل النمو الوعائي البطاني،مرضى الصدفية،مؤشر المساحة والشدة للصدفية.

Introduction

Psoriasis is a common inflammatory autoimmune disease influencing about 1-3% of the overall population, it is a multifactorial disorder caused by polygenic inheritance and environmental triggers, such as infections, drugs or trauma.Angiogenesis is recognized to be a vital pathogenic component of psoriasis. Lastly there is promptly developing understanding of the cellular processes causing inflammation in psoriasis. Vessel expansions appears to act a significant function in the progression of psoriatic plaques [1,2].

The key factor accountable for angiogenesis in various tissue is VEGF as it is an extremely specific mitogen for endothelial cells.Vascular endothelial growth factor is a chief controller of physiologic and pathologic neoangiogenesis.Overexpressions of VEGF could upregulate angiogenesis, in psoriatic, skin when dominates the action of antiangiogenics factor and it is responsible on the chronicity in psoriasis lesions [3-6]. Researches showed that in the skin vascular endothelial growth factor was produced primarily by keratinocytes and its' concentrations is increased in the affected as well as unaffected skin of psoriatic patients [6].

The onset of psoriasis occurrence is at any age, involvingbirth, even so there are two peaks, first about 15-20 years old, and the other is about 55-60 years old .There are insignificant variations in the incidence of psoriasis in male and female patients [7]. Psoriasis vulgaris is the commonest type of psoriasis, contributing approximately 90% of all psoriatic patients. Psoriasis is characterized by sharply demarcated, erythematous, scaly plaques of different sizes. Psoriatic lesions are classically spread in symmetrical fashion, and found frequently on the extensor parts of elbows and knees, scalp, lumbosacral region, and umbilicus [8].

The objective of study is toevaluate the level of serum vascular endothelial growth factor and its correlation with PASI score in psoriatic patients.

Materials and Methods

This is a case-control study which included 150 subjects (100 patients and 50 controls) who attended different medical centers including Al-Sadr Medical City and department of laser research in AL-Najaf city and Marjan Medical City in AL-Hilla city from November/2013 to January /2015. Informed consents were gained from participant. The practical's parts of this study were done at the Biology Dept/College of Science/Babylon University.

The inclusion criteria include,consenting, patients having chronic plaque psoriasis with PASI score > 20 aged between 20 to 60 years with no co morbid illness or any medications.

After informed written consent, Psoriasis Area Severity Index (PASI) scoring was estimated [9].

The groups of the patients are as the following (figure 1):

1- Group I: Includes 20 males whose age ranged from 20 to 39 years .
2- Group II: Includes 33 females whose age ranged from 20 to 39 .
3- Group III:: Includes 23 males whose age ranged from 40 to 60 years.
4- Group IV: Includes 24 females whose age ranged from 40 to 60 years .

A uniformed cases sheets were assigned for every participant in the study which includes:

1. Age of the patient.
2. Gender of the patient.

sVEGFMeasurement

Eight to ten milliliters of blood were collected in plane tube without anticoagulants , the tubes were left for 30 minutes at room temperatures. After coagulation, tubes were centrifuge at 1000 xg for about 15 minutes, the serum was extracted and allocated into three parts,and kept at (–20º C) till usage time.

Serum aliquots were obtained to measure sVEGFbysensitive Enzyme Linked Immuno Linked Sorbant Assay technique (ELISA)using ABCAM Human VEGF ELISA Kit[10].

Statistical Analysis

Statisticalcanalysis were done by SPSS 20.0 (SPSS Inc, Chicago, I L, USA).

The normal distribution was confirmed for all analyzed measures. For correlation analysis, independent t-test is utilized to evaluate difference between two group in continuous variable.ThePearson's product moment correlation was used and the binary logistic regression analysis used to determine the odds ratio[11].

Results

In the present study,A total of 100 patients were included in the study with 43(43%) males and 57 (57%) females (Figure1). The males to females ratio was1:1.3.

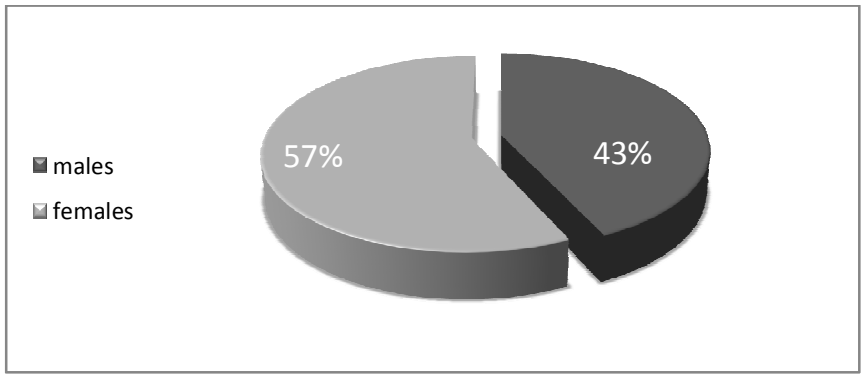

Figure 1: Gender wise distribution of study patients**.**

Among the studied 100 patients, 53 (53%) patients were in the age group of 20–39years and 47 (47%) patients were in the age group of 40-60 years (figure 2).

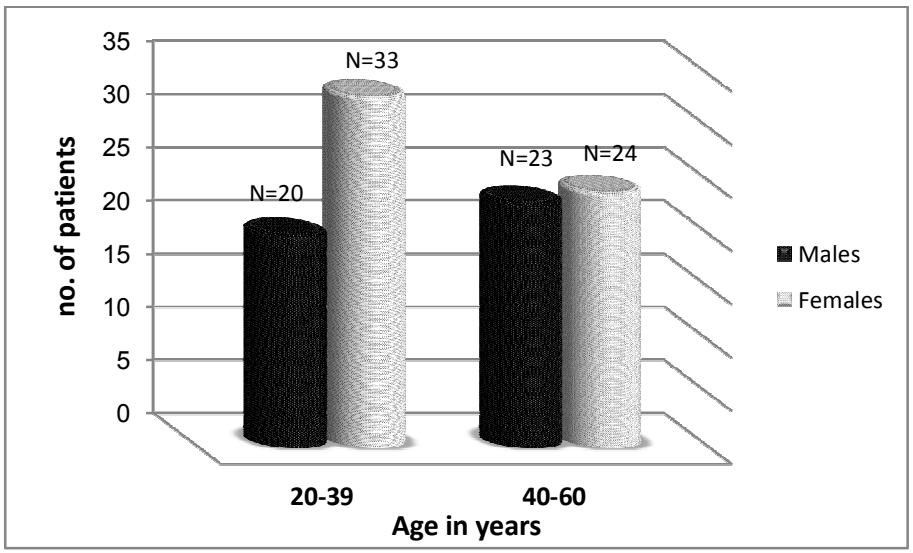

Figure2: Age wise distribution of study patients.

All patients presented severe forms of psoriasis vulgaris as shown by psoriasis areas and severity index (PASI) score (mean ±SD) of35.85 ± 9.45 with range (20.76-51.97).

Psoriatic patient showed numerous significant disturbance, as compared to control, namely higher level of sVEGFfor males(P value is 0.00013) and females (P value is 0.00041) with age group between (20-39years)and males(P value is 0.0001) and females (P value is 0.00032) with age group between (40-60years) (P<0.001) (figure 3 and figure 4) .

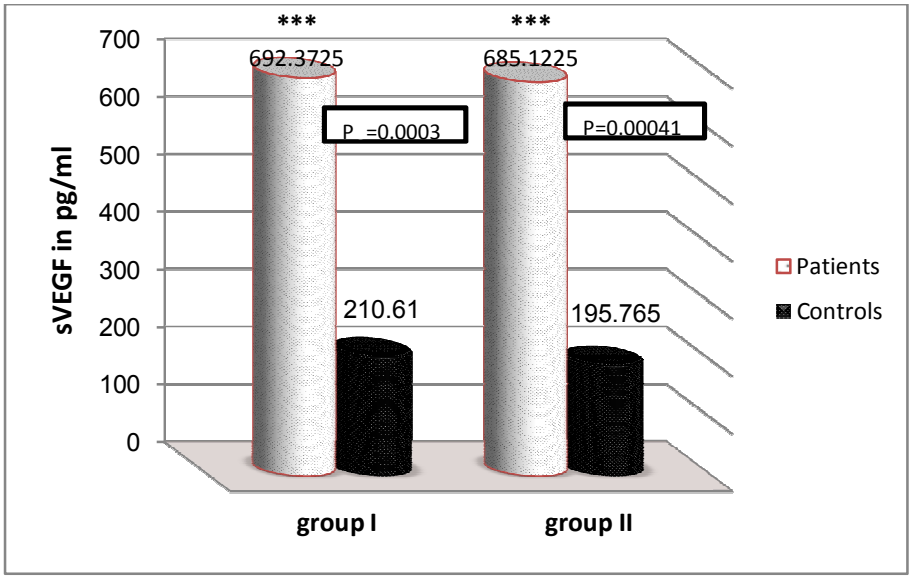

Figure 3 : Vascular endothelial growth factor for males and females with age group between 20-39years(groups I and II).
sVEGF : serum vascular endothelial growth factor.
*** Significant differences at P<0.001.

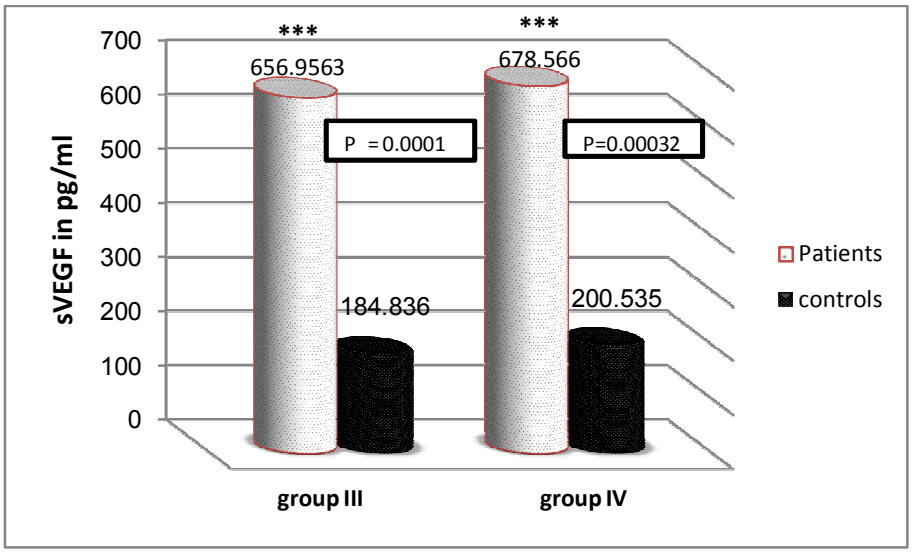

Figure4: Vascular endothelial growth factor for males and females with age group between 40-60years (groups III and IV).
sVEGF : serum vascular endothelial growth factor.
***Significant differences at P<0.001.

The serum level of vascular endothelial growth factor showed insignificant differences between males and males as well as between patients in the two ages groups (Table 1).

Table1: Mean values (±SD) of serum vascular endothelial growth factor (VEGF) concentration according to age and sex

Parameter	sVEGF (Mean ±SD)		Pvalue
Sex	males	674.3598±191.869	0.836
	females	682.4513± 190.35818	
Age (in years)	20-39	688.68±185.687	0.587
	40-60	667.5213± 196.5	

sVEGF : serum vascular endothelial growth factor.

Significant correlations were established between sVEGF serum concentration and psoriasis area and severity index score.

Table 2:correlations (expressed as r-value) of psoriasis areas severity index (PASI) and serum vascular endothelial growth factor (sVEGF)

Parameters	(Means ±SD)		sVEGF
PASI score	**35.853 ± 9.453**	**r**	**0.784**
		P	**0.022***

sVEGF : serum vascular endothelial growth factor

*Statistically significant ($P < 0.05$) correlations ; r correlation coefficient.

Discussion

The present study showed a slightly female predominance (male/female ratio approximately 1:1.3) which yet again may reflect a sex related preference in psoriatic patients (figure 1). This was in accordance to Mallbris (2005) who found a female dominance (approaching 1.3:1) as compared with the male[12].

Several researchers reported that psoriasis occurs in any gender or race with equal amount of male and female [13,14]. There is remaining controversy regarding psoriasis gender preponderance and it lies between no difference [15] to male preponderance [16]. In one research, no gender difference were observed in the frequency of items related to appearance and socialization [17].

Additionally, in united states the overall, yearly crudes incidences rates were 57.6per100000 populations; regarding the males, the incidence was54.4per 100000 and concerning the females, it was 60.2 [18]. In contrast earlier reports had detected eithersan equals incidenceor slightly males predominance amongst psoriatic patients[19]. Hwertaand his coworkers (2007) andLafi and his coworkers (2010) showed males were more affected with psoriasis in all age groups studied[20,21].

In this study, psoriasis was found to be higher in patients of age groups 20-39 years old; the number of the patients in this age group 53/100(53%) as shown in figure 2. This result corresponds to an Egyptian study which mentioned that

psoriasis was higher in individuals of age group 18-40 years old (62.8%). This finding was also in accordance with what was detected by Hwertaand his coworkers (2007) andZieve and his coworkers (2008)[20,22].

Concerning sVEGF, our results suggest that there is highly significant increment in sVEGF in all psoriatic patients compared to control (Figures3and4).

Our findings are compatible with the finding of other several authors who reported that its levels are significantly high in plasma in the active stage of the disease [23-26]. Nonetheless, Shimauchi*et al* (2013) did not find significant differences in VEGF levels between psoriasis patients and controls[27]. Flisiak and his coworkers (2010) and Flisiak and his coworkers (2012) reported that the increase of serum VEGF becomes significant only in psoriatic patients with severe, type of psoriasis[28,29].

Flisiak and his coworkers (2010), Flisiak and his coworkers (2012)andTakahashi and his coworkers(2010) found a positive correlation between psoriatic activity and serum vascular endothelial growth factor[28-30]. According to Creamer and his coworkers (2002) patients with moderate to severe, type of psoriasis-, means serum VEGFlevelthroughoutthe exacerbation of the symptoms were two time higher than throughout remissions and there were a direct correlations between VEGF, levels in serum and psoriasis severity in addition to the occurrence of psoriatic arthritis(PsA)[31]. Fink and his coworkers (2007) established the average VEGF, levels in serum concentrations in psoriatic patients with PsA were practically twice times more than that inpsoriatic,patients,with exacerbateddiseases and controls[32]. Consequently they established serum,VEGF,is a moral sign of exacerbated PsA. Nofal and his coworkers (2009) confirmed aconsiderableelevation of serum, VEGFin patients with psoriasis and its important correlations with PASI scores[33].

Concerning the sex and age, there are no significant changes in serum level of VEGF between males and females along with between patients in age group20-39 and patients in age group 40-60 ($P>0.05$) (Table 1). These results are in accordance with the results of Flisiak and his coworkers (2012). Our results agreed with the finding of Flisiak and his coworkers (2010) [28] and disagree with the finding of Creamer his coworkers (2002) who said that high plasma levels of VEGF-A are associated with early onset psoriasis (onset before the age of 40 years) and psoriatic arthritis[31]. This findings mean that the level of VEGF don't affected with age as well as with the sex of the patients.

In conclusion,serum vascular endothelial growth factor significantly increase in psoriatic patient and its level is significantly correlated with PASIscore and its level don't affected by age or the sex of the patients.

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