Egyptian Journal of Medical Research (EJMR)

Usefulness of Vaspin Marker and C-reactive Protein in Assessment of the Severity of Psoriasis

Aya Emad Eldin Mohamed Sadek [a], Abd El-Aziz El Rifaie [b] , Laila Ahmed Rashed [c] and Rehab Mohamed Naguib [b]

a. Dermatology department Elwasta central hospital, Ministry of health

b. Dermatology department, Faculty of Medicine, Beni-Suef University, Egypt

c. Biochemistry department, Faculty of Medicine, Cairo University, Egypt.

Abstract:

This study aims to study the level of Vaspin and CRP in the serum of psoriatic patients as compared to normal control persons and to correlate their levels with the severity of the disease. **Methods:** 30 psoriasis patients as cases vs 30 normal patients as control were tested for CRP and Vaspin correlating the results with the Psoriasis Severity Index PSI. **Results:** There was a highly statistically significant difference between cases and controls regarding their VASPIN and CRP levels (P-value<0.001). in cases there was a significant positive moderate linear correlation between CRP and PASI. There was a significant strong negative linear correlation between the VASPIN and the PASI score (P-value=0.009), showed that at a cut off 75.6 of vaspin predicted that the patient had no psoriasis with 100% sensitivity and 75.6% specificity. **Conclusions:** CRP and Vaspin could be used as markers to assess the severity of the disease and treatment response.

Keywords: Psoriasis, Vaspin, CRP.

1. Introduction:

Psoriasis is a common, chronic, inflammatory skin disease that results from a polygenic predisposition combined with triggering factors, e.g. trauma, infections or medications [1].

Psoriasis was described at the early medicine in the *Corpus Hippocraticum*. Hippocrates and his school (460–377 BCE) characterized many skin disorders. They calcified dry, scaly eruptions under group "lopi". probably included psoriasis and leprosy [2].

The important clinical hallmarks are: erythema, thickening and scaling. The plaque type of psoriasis is the most common type [2].

The typical history includes itching, skin redness and scaling. Patients may report

that their disease worsens in the winter and improves in the summer [3].

The seriousness of psoriasis may be assessed differently by each patient and physician.The Psoriasis Area and Severity Index is often used in clinical trials to quantify the biological severity of psoriasis at a given point in time (PASI).

This is a composite score incorporating a grading of erythema, induration and scaling of plaques, multiplied by the surface area of the skin involved. This score has been validated in the clinical setting and although it has many shortcomings, it remains the gold standerd tool for psoriasis assessement [4].

Patients with psoriasis are more prone to cardiovascular disease (CVD), stroke, lymphoma and non-melanoma skin cancers. The severity of skin lesions tends to be related to the risk of developing significant co-morbidities including myocardial infarction (MI). Young adults with serious psoriasis have a three-fold increased risk of MI and a life expectancy drop of three to four years [5].

CRP is a homopentameric acute-phase inflammatory protein that is upregulated in inflammatory conditions like rheumatoid arthritis, cardiovascular disease, and infection [6].

Vaspin (Visceral Adipose tissue-derived Serpin) is an adipocytokine isolated from Otsuka Long-visceral Eva's adipose tissue. It belongs to the serine protease inhibitor class [7].

In humans; Vaspin expression has been found in visceral and subcutaneous white adipose tissue interestingly, a relatively high expression of VASP mRNA has been found in the skin [8].

Furthermore, the serum concentrations of VASP have been shown to be higher in women than in men with normal glucose tolerance [9].

This study aims to assess the level of Vaspin and CRP in the serum of psoriatic patients as compared to normal control persons and to correlate their levels with the severity of the disease may help to assess disease severity and follow up its course that is what we are focusing on in this thesis.

2. Patients and Methods:

2.1Type, site and time of study:

This is a case control study that included 60 patients segregated into two groups:

30 patients with psoriasis and 30 relatively normal as control. The study was approved by the ethical committee of faculty of medicine Beni-Suef University

2.2 Inclusion and exclusion criteria:

1 -Inclusion criteria

1. Age between 18 to 75 years old.
2. Patient with chronic plaque psoriasis.
3. Both males and females were included

.2 -Exclusion criteria

1. Pregnant and lactating females
2. Age below 18 years old and above 75.
3. Patients diagnosed with other autoimmune disease.
4. Patients with acute infection at time of sample taking.
5. Patients with associated other dermatological diseases.

2.3 All patients were subjected to:

•An informed consent was signed by each patient before enrolment in the study.

•Personal history: Name, age, sex, skin type, occupation, residence, marital status and smoking.

•History of present illness: Onset, course, duration of disease, precipitating factors and any medications.

•Family history of psoriasis

•Past history of any associated systemic or dermatological diseases.

•Drug history.

•Blood sample: 3 ml venous blood was withdrawn from all patients and controls centrifuged for 15 minutes, then stored at -20 oC for ELISA examination for vaspin and high sensitive CRP

Study subjects:

1- Psoriatic patients; group were subjected to

•Clinical assessment: to determine extent of psoriasis (%) and the disease severity.

•Assessment of severity: PASI score was used the PASI score is the most commonly used tool to assess disease severity in patients with psoriasis in clinical trials. The PASI measures erythema, scaling, and thickness of lesions and is weighted by the area of involvement. The head, trunk, upper and lower extremities are the areas assessed. The PASI scale ranges from 0 to 72, calculated as the extent of involvement × (score for erythema + score for scaling + score for thickness), where the extent of involvement is categorized as: 0 (0%), 1 (1–9%), 2 (10–29%), 3 (30–49%), 4 (50–69%), 5 (70–89%), or 6 (90–100%), and scores for erythema, scaling, and thickness are each rated on a scale of 0 to 4.

2- Control group:

30 healthy subjects were included as control group. All recruits were above 18 years with no history of chronic dermatological or systemic disease including renal, liver diseases or malnutrition.

2.4 Statistical analysis:

Data analysis was performed using SPSS v. 25 (Statistical Package for Social science) for Windows. Description of quantitative variables was done in the form of mean, standard deviation (SD), description of qualitative variables was done in the form of numbers (No.) and %. Comparing between quantitative variables was carried out by independent t-test that was used to test the difference between the means of 2 groups of a scale variable. Comparing between categorical data was done using the Chi square test, to test the statistical difference between the 2 groups.

Correlation was done to test the association between 2 scale variables. The significance of the results was assessed in the form of P-value that was differentiated into non-significant when P-value > 0.05 and significant when P-value ≤ 0.05.

2.5 Ethical Considerations and Review:

Study protocol was approved by Faculty of Medicine, Beni-Suef University, Research Ethics Committee.

3 .Results:

As summarized in Table 1, baseline characteristics, such as gender, age, were not significantly different between thcase and controle groups (all P>.05). [Table (1)].

[Table (1)]: *baseline characteristics of cases and controls.*

Characteristics	Cases N=30 no.(%)	Controls N=30 no.(%)	P-value
Age:			
Mean ± SD	46.1±13.8	47.7±6.6	0.597
Range(min-max)	(18-75)	(32-58)	
Median	47	48	
Sex:			
Males	19(63.3)	15(50)	0.297
Females	11(36.7)	15(50)	

As shown in Table (2) the most of cases had gradual onset of psoriasis (93.3%), more than half of them had remission and exacerbation episodes (56.7%) and the most common precipitating factor was cold (46.7%). The mean of the duration of the disease was 109.9±87.9 months and the PASI mean was 8.1±6.4.

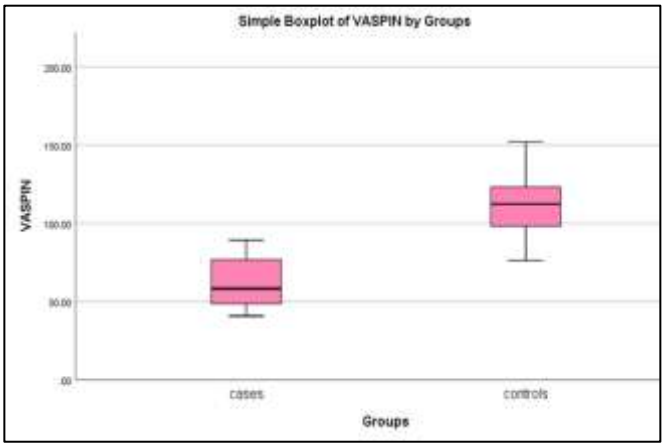
Comparison between cases and controls regarding the VASPIN and CRP levels:

showed that Mean of VASPIN among cases was 63.4±16.5 and that of controls was 110.7±16.9 but CRP of cases was 4.8±2 and that of controls was 2.2±0.82. There was a highly statistically

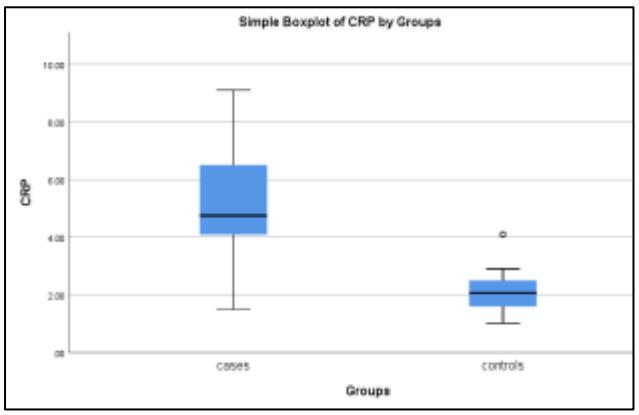
significant difference between cases and controls regarding their VASPIN and CRP levels (P-value<0.001) Figure (1-2).

[Table (2)]: *disease characteristics*

Disease Criteria	Number N=30	Percent 100%
Onset:		
Gradual	28	93.3
Sudden	2	6.7
Course:		
progressive	7	23.3
stationary	4	13.3
regressive	2	6.7
remission &exacerbation	17	56.7
Precipitating factors:		
cold and stress	6	20.0
cold	14	46.7
stress	9	30.0
sun	1	3.3
Duration of the disease(month):		
Mean±SD	109.9±87.9	
Range(min-max)	(1-260)	
Median	120	



[Figure (1)]: *Comparison between cases and controls regarding the VASPIN level.*



[Figure (2)]: *Comparison between cases and controls regarding the CRP levels .*

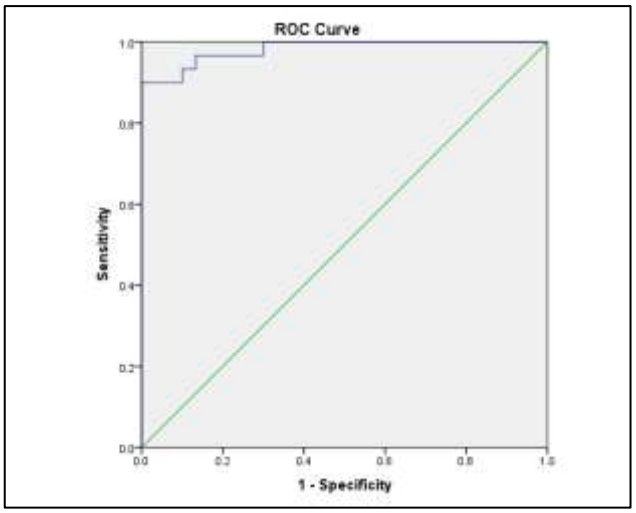
Correlation between VASPIN & CRP and different factors (age, PASI and disease duration)

As shown in table (3) there was a significant positive moderate linear correlation between CRP and age of both cases and controls also in cases there was a significant positive moderate linear correlation between CRP and PASI.

There was a significant strong negative linear correlation between the VASPIN and the PASI score (P-value=0.009)

ROC Curve analysis for prediction of psoriasis:

As shown in Figure (4) and table (4) ROC curve analysis showed that at a cut off 75.6 of vaspin predicted that the patient had no psoriasis with 100% sensitivity and 75.6% specificity.



[Figure (3)]: ROC curve analysis cut off value for vaspin as a predictor of absence of psoriasis.

[Table (3)]: correlation between VASPIN & CRP and different factors (age, PASI and disease duration).

Groups			**VASPIN**	**CRP**
Cases	Age	r	-0.293	0.440*
		P-value	0.116	0.015
	PASI	r	-0.617**	0.492**
		P-value	0.009	0.006
	Disease duration	r	0.181	0.278
		P-value	0.337	0.136
controls	Age	r	0.142	0.448*
		P-value	0.454	0.013

r=correlation coefficient *P-value is significant.

4. Discussion:

CRP is a homopentameric acute-phase inflammatory protein that is upregulated in inflammatory conditions like rheumatoid arthritis, cardiovascular disease, and infection [6]. Vaspin (Visceral Adipose tissue-derived Serpin) is an adipocytokine isolated from Otsuka Long-visceral Eva's adipose tissue. It belongs to the serine protease inhibitor class [7].

In humans; Vaspin expression has been found in visceral and subcutaneous white adipose tissue interestingly, a relatively high expression of VASP mRNA has been found in the skin [8].

Furthermore, the serum concentrations of VASP have been shown to be higher in women than in men with normal glucose tolerance [9].

A great deal of researchs had addressed the elevation of C-reactive protein (CRP) Vaspin (Visceral Adipose tissue-derived Serpin) among psoriatic patients and the role of these markers in assessment of disease severity and progression.

In order to study the level of Vaspin and CRP in the serum of psoriatic patients as compared to normal control persons and to correlate their levels with the severity of the disease we included 60; patients 30 cases and 30 controls we found that

The demographic data of our patients showed that mean age of the studied case is 46.1±13.8 and controls 47.7±6.6), males and females ratio were 63.3% and 36.7% respectively and 50% 50% in controls, there was no statistically significant difference between cases and controls regarding their age and sex.

This is in agreement with Hilal Gökalp,et al who studied 62 patients consisted of 31 (50%) females and 31 (50%) males. The age ranged from 18 to 69 years with mean age 41.74±13.96 years. No statistically significant difference was found between the psoriasis patient group and the control group in terms of gender and age [10].

Exploring the impact of psoriasis on CRP we correlated the level of CRP with psoriasis patients and controls showed that there was a

highly statistically significant difference between cases and controls regarding CRP levels (P-value<0.001).

CRP of cases was 4.8±2 and that of controls was 2.2±0.82., in other words, higher levels of CRP were correlated with psoriasis this was in the same context with Serwin AB who reported increased CRP concentrations in active psoriasis [11].

Also, our results go hand in hand with study done by Uysal S identified CRP as a marker for psoriasis severity [12].

Also Isha et al, found that CRP levels increased by more than 20 times in psoriasis patients compared with the healthy individuals. After 12 weeks of treatment, it fell to nearly 50% of the initial value [13].

Our results also coincides with the study done by Biljan et al, conducted in 70 psoriasis patients, observed that inflammatory parameters such as CRP serum levels were significantly related to the clinical demonstrations of psoriasis (p<0.005). They also identified a relationship between disease severity and the increased levels of inflammatory reactions [14].

In our study we tested the usefulness of CRP as a marker of psoriasis severity that could be used to monitor psoriasis and its treatment, and, together with PASI it showed that there was a significant positive moderate linear correlation between CRP and PASI

This was in agreement with a cross-sectional study conducted on 73 psoriasis patients, Coimbra et al noted that CRP serum levels were related to PASI scores and that they could be reduced by using NB-UVB as a treatment. Consequently, it is suggested that CRP serum levels can be considered a useful marker for diagnosing psoriasis severity and monitoring disease activity or the disease's reaction to treatment [15].

In another study of 175 male psoriasis patients performed by Chodorowska et al, the clinical activity of psoriasis was calculated based on the PASI score, which reflected the increase in CRP serum levels during the acute phase (P<0.001) [16].

Similary Strober et al investigated the etanercept effects on CRP serum levels and observed increased CRP serum levels in patients with moderate to severe plaque-type psoriasis who were suffering from systemic inflammation. The activity of the skin disease was accompanied closely by improvement in serum CRP levels [17].

Our results are side by side to Kanelleas et al, analyzed the role of inflammatory markers among psoriasis patients to evaluate the severity of the disease and its response to treatment. Furthermore, they found that inflammatory markers such as CRP serum levels diminish post-treatment (P<0.001) and identified a relationship between PASI scores and CRP. Due to this

relation, inflammatory markers, especially CRP, can be used to evaluate the severity of psoriasis and its response to treatment. In addition, the inflammatory markers, together with the PASI score, may represent an inflammatory situation for psoriasis [18].

Regarding vaspin our results showed that there was a highly statistically significant difference between cases and controls regarding their VASPIN (P-value<0.001 .(Mean of VASPIN among cases was63.4±16.5 and that of controls was 110.7±16.9.

Similarly, to another study, conducted by Saalbach et al., the researchers have confirmed a markedly decreased expression of VASP within the epidermis of psoriatic lesions in comparison to the skin of healthy individuals. They have also found that the expression of the adipokine in keratinocytes is correlated with the differentiation of keratinocytes and decreases under the influence of pronounced proliferation and stimulation by pro-inflammatory factors such as TNF-α, IL-17, IL-20, IL-6, i.e. processes involved in the pathogenesis of psoriasis. The authors claim that the expression of VASP in keratinocytes takes part in reducing inflammation in the skin and may play a significant role in the emergence of chronic inflammatory skin diseases, one of them being psoriasis [19].

In our study there was a significant strong negative linear correlation between the VASPIN and the PASI score (P-value=0.009)

This was in agreement with Ataseven A1, Kesli R who studied A total of 56 patients suffering from psoriasis and 34 age-matched controls were included. Vaspin, VAP-1, YKL-40, and hs-CRP serum levels were evaluated by ELISA. The psoriasis area severity index (PASI) was calculated in all psoriatic patients and patients were divided in two groups according to PASI <10 or ≥10 she found that the serum concentration of vaspin was the only marker to exhibit a significant difference between the low and high PASI groups (1.40±0.27 pg/mL and 1.20±0.37 pg/mL, respectively; P<0.05 [20].

Finally we were able to define a cut off value of vaspin equals 75.6 above which the patient had no psoriasis with 100% sensitivity and 75.6% specificity.

5. Conclusion:

- There is a highly statistically significant difference between cases and controls regarding their VASPIN and CRP levels
- There is a significant positive moderate linear correlation between CRP and PASI.
- There is a significant strong negative correlation between the VASPIN and the PASI score (P-value=0.009)
- CRP and Vaspin could be used as markers to assess the severity of the disease and treatment response.

6. References:

1- Roberson, E.D., Bowcock, A. M. (2010). Psoriasis genetics: breaking the barrier. Trends in Genetics, 26(9), 415-423.

2- Nickoloff, B. J., & Nestle, F. O. (2004). Recent insights into the immunopathogenesis of psoriasis provide new therapeutic opportunities. The Journal of clinical investigation, 113(12), 1664-1675.

3- Lui, H. and Mamelak, A.J. (2009): Psoraisis. Emedicine. Medscape.com.

4- Finlay, A.Y. (2005). Current severe psoriasis and the rule of tens. British Journal of Dermatology, 152(5), 861-867.

5- Mehta, N. N., Li, K., Szapary, P., Krueger, J., & Brodmerkel, C. (2013). Modulation of cardiometabolic pathways in skin and serum from patients with psoriasis. Journal of translational medicine, 11(1), 1-8.

6- Du Clos, T. W., & Mold, C. (2004). C-reactive protein. Immunologic research, 30(3), 261-277.

7- Lago, F., Dieguez, C., Gómez-Reino, J., & Gualillo, O. (2007). Adipokines as emerging mediators of immune response and inflammation. Nature clinical practice Rheumatology, 3(12), 716-724.

8- Heiker, J. T. (2014). Vaspin (serpinA12) in obesity, insulin resistance, and inflammation. Journal of Peptide Science, 20(5), 299-306.

9- Youn, B. S., Klöting, N., Kratzsch, J., Lee, N., Park, J. W., Song, E. S., ... & Blüher, M. (2008). Serum vaspin concentrations in human obesity and type 2 diabetes. Diabetes, 57(2), 372-377.

10- Gökalp, H. (2018). Effect of psoriasis severity on inflammation parameters: controlled study. Turk J Dermatol, 52.

11- Serwin, A.B., Wasowicz, W., & Chodynicka, B. (2006). Selenium supplementation, soluble tumor necrosis factor-α receptor type 1, and C-reactive protein during psoriasis therapy with narrowband ultraviolet B. Nutrition, 22(9), 860-864.

12- Uysal, S., Yilmaz, F. M., Karatoprak, K., Artuz, F., & Cumbul, N. U. (2014). The levels of serum pentraxin3, CRP, fetuin-A, and insulin in patients with psoriasis. Eur Rev Med Pharmacol Sci, 18(22), 3453-8.

13- Jain, V. K., & Lal, H. (2011). C-reactive protein and uric acid levels in patients with psoriasis. Indian journal of clinical biochemistry, 26(3), 309-311.

14- Biljan, D., Šitum, M., Kostović, K., Batinac, T., & Matišić, D. (2009). Acute phase proteins in psoriasis. Collegium antropologicum, 33(1), 83-86.

15- Coimbra, S., Oliveira, H., Reis, F., Belo, L., Rocha, S., Quintanilha, A& Santos-Silva, A. (2010). C-reactive protein and leucocyte activation in psoriasis vulgaris according to severity and therapy. Journal

of the European Academy of Dermatology and Venereology, 24(7), 789-796.

16- Chodorowska, G., Wojnowska, D., & Juszkiewicz-Borowiec, M. (2004). C-reactive protein and α2-macroglobulin plasma activity in medium–severe and severe psoriasis. Journal of the European Academy of Dermatology and Venereology, 18(2), 180-183.

17- Strober, B., Teller, C., Yamauchi, P., Miller, J. L., Hooper, M., Yang, Y. C., & Dann, F. (2008). Effects of etanercept on C-reactive protein levels in psoriasis and psoriatic arthritis. British Journal of Dermatology, 159(2), 322-330.

18- Kanelleas, A., Liapi, C., Katoulis, A., Stavropoulos, P., Avgerinou, G., Georgala, S & Katsambas, A. (2011). The role of inflammatory markers in assessing disease severity and response to treatment in patients with psoriasis treated with etanercept. Clinical and Experimental Dermatology: Clinical dermatology, 36(8), 845-850.

19- Saalbach, A., Tremel, J., Herbert, D., Schwede, K., Wandel, E., Schirmer, C., ... & Simon, J. C. (2016). Anti-inflammatory action of keratinocyte-derived vaspin: relevance for the pathogenesis of psoriasis. The American journal of pathology, 186(3), 639-651.

20- Ataseven, A., & Kesli, R. (2014). Novel inflammatory markers in psoriasis vulgaris: vaspin, vascular adhesion protein-1 (VAP-1), and YKL-40. Giornale italiano di dermatologia e venereologia: organo ufficiale, Societa italiana di dermatologia e sifilografia, 151(3), 244-250.