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Assessment of Serum Level of Chitinase-3-Like-Protein 1 among Psoriatic Patients

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ABSTRACT
Background: psoriasis is a chronic inflammatory autoimmune skin disorder, with a high relapse rate. The etiology and pathogenesis of psoriasis are still unclear. Many cytokines produced by inflammatory cells give rise to the induction and maintenance of psoriatic plaques. YKL-40 or chitinase 3-like protein1(CHI3L1) may be involved in angiogenesis in psoriasis which has an important role in the pathogenesis of the disease.
Objectives: The aim of this study was to study the serum level of YKL-40 in patient with psoriasis in order to assess its possible role in pathogenesis and severity of the disease.
Patients and method: this study included 60 psoriatic patients and 30 healthy subjects of matched age and sex, served as a control group. Blood samples were taken from all patients and controls for estimation of serum level of YKL-40 by ELISA.
Results: A statistically significant increase in median serum YKL-40 level in psoriatic patients compared with control group. A positive correlation between serum YKL-40 and severity of psoriasis according to PASI score.
Conclusion: serum YKL-40 can be used as a new marker for evaluation of disease severity, progression and therapeutic decision in psoriasis.
Keywords: Arachidonic acid, Endothelial dysfunction, Epidermal growth factor receptor

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease that affects 2-3% of the world's population [(1, 2)]. Classical psoriasis is also known as chronic psoriasis or psoriasis is the most common type. It can be diagnosed fairly easily as distinct red plaques with well-defined borders and silver-white dry scales, found in the elbows, knees and scalp, although they can be more comprehensive. Other less common types of psoriasis also occur, such as raster, Pimples, rheumatic psoriasis and arthritis [(3, 4)].

The cause of psoriasis is unknown, although it is generally thought to be a complex inflammatory disease with a genetic and immune basis that can be altered by many environmental factors such as stress, weather, physical trauma, medication and infection [(5)].

Psoriasis is characterized by excessive growth of the epidermal keratinocytes, inflammatory cell accumulation and excessive dermal angiogenesis [(6)].

YKL-40 or chitinase 3-like protein1(CHI3L1) is a member of 18 glycosyl hydrolases (mammalian chitinase) family.YKL-40 is one of the major secreted proteins from human articular chondrocytes, synovial cells, endothelial cells and macrophages [(7)].

The exact biological functions of YKL-40 are unknown. However, it is suggested that it participate in the physiological and pathological processes such as angiogenesis, mitogenesis and remodeling [(8)]. It is expressed and secreted by cancer cells of different origins along with avariety of non-malignant cells including inflammatory and structural cells. Thus, it is implicated in cancers, cardiovascular diseases, infections and other disorders [(9)].

Serum levels of YKL-40 are increased during tissue remodeling and in a variety of inflammatory conditions, such as rheumatoid arthritis, chron's disease and cancers. According to the role of YKL-40 in inflammatory diseases, we will study serum YKL-40 in psoriasis [(10)].

The aim of this work was to study the serum level of chitinase -3-like- protein 1 (YKL-40) in patient with psoriasis in order to assess its possible role in pathogenesis, severity and therapeutic approach of psoriasis.

PATIENTS AND METHODS

This study included a total of 60 psoriatic patients and 30 normal healthy individuals with

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matched age and sex, served as a control group, attending at Outpatient Clinic of Dermatology and Venereology Department, Al-Azhar University (Damietta).

Approval of the ethical committee and a written informed consent from all the subjects were obtained.

- **Inclusion criteria:** Patients with psoriasis who didn't receive any systemic treatment for the last 3 months.
- **Exclusion criteria:** Recent infection. Any disease or drug affecting serum Chitinase level: Rheumatoid arthritis, malignancies, etc. Any patients receiving systemic treatment or phototherapy for psoriasis for the last 3 months.

All participants were subjected to the followings:

Clinical evaluation: Complete history taking: Personal, present and family. Past history of psoriasis. Drug history (systemic or phototherapy). **Thorough** general and dermatological examination to exclude any systemic or other dermatological diseases that may affect serum (YKL- 40). Detailed dermatological examination of the lesion to assess: distribution, morphology, PASI score. PASI score calculation for assessment of psoriasis severity is a score that evaluate the severity of psoriasis in relation to (four) parameter including erythema (redress) (R) infiltration (thickness) (T), desquamation (scaling) (S) and body surface area involvement (A) as in table (2). Severity is matted for each index on (0-4) scale (0) for no involvement up to (4) for severe involvement [11].

The body is divided into four regions comprising the head (H), upper extremities (U), trunk (T) and lower extremities (L) as in table (3). In each of these areas, the fraction of total surface area affected is graded on a 0-6 scale (0) for no involvement up to (6) for greater than 90% involvement [12].

Table (1) PASI score calculation [11]**:**

Score	**0**	**1**	**2**	**3**	**4**	**5**	**6**
Erythema Induration Desqaumation	None	Mild	Moderate	evere	y severe	-	-
Area %	0	10%	10-30%	)-50%	)-70%	0-90	)-100

Table (2): Body surface area assessment [12]:

Head	H	10%
extremities	U	20%
	T	30%
extremities	L	40%

The composite PASI score can then be calculated by multiplying the sum of the individual-severity scores for each region by the weight of area of involvement score for the respective region, and then summing the four resulting quantities;so PASI score is calculated by the following formula:

PASI = 0.1 (Rh + Th + Sh) Ah + 0.2 (Ru + Tu + Su) Au + 0.3 (Rt + Tt + St) At + 0.4 (Rl + Tl + Sl) Al

The patients were divided in to three groups according to PASI score:

- **Group A (mild):** Including patients with psoriasis of mild severity (PSAI score <10).
- **Group B (moderate):** Including patients with psoriasis of moderate severity (PSAI score 10 up to 30).
- **Group C (severe):** Including patients with severe form of psoriasis (PSAI score more than 30).

Laboratory investigations:

1. **Routine laboratory investigations:** Including complete blood count (CBC), fasting and postprandial blood sugar levels and liver and renal function tests.
2. **Estimation of the serum YKL-40 level by enzyme linked immunosorbent assay (ELISA).**

Statistical analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science and analyzed using IBM SPSS software package version 20.0. Quantitative data were described using range median (minimum and maximum), mean, and standard deviation. Qualitative data were described as number and percentage.**The used tests were:** ***Student t test, Chi-Square test*** for comparison of qualitative variables. **Receiver operating characteristics** was used for calculation of validity of YKL-40 for detection of best cut off point, **Cross tabulation** was used for calculation of Positive predictive, Negative predictive and Accuracy values and **Spearman correlation coefficient**. **Level of significance**: for all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (p-value). All tests were 2 tailed. **The results was considered:** Non-significant when the probability of error is more than 5% ($p > 0.05$). Significant when the probability of error is less than 5% ($p < 0.05$).

The ROC curve **(receiver operating characteristic)** provide a useful way to evaluate the sensitivity and specificity for quantitative diagnostic measures that categorize cases in to one of two groups.

RESULTS

Table (3): Comparison of demographic characters between studied groups

Demographic characteristics	Cases n=60	Control n=30	Test of significance
Age/years			t=0.21
Mean ± SD	38.43±18.21	39.30±18.19	P=0.83
Sex No. (%)			
Male	35(58.3)	18(60.0)	χ^2=0.02
Female	25(41.7)	12(40.0)	p=0.88

t:Student t test χ^2:Chi-Square test p:probability

Table (3) show that the present study was carried out on 60 psoriasis patient. Their mean age 38.43±18.21, they were 35 male (58.3%) and 25 female (41.7%) . in addition to 30 healthy control individauls of matched age and sex (p>0.05).

Table (4): Comparison of YKL-40 between studied groups.

	Cases n=60	Control n=30	Test of significance
YLK-40 (ng/ml)	49.71	37.24	Z=6.1
Median (Min-Max)	(16.37-201.0)	(35.0-48.42)	P<0.001*

Z:Mann-Whitney U test p:probability *statistically significant (p<0.05)

Table (4) show that the illustrates that there is statistically significant difference between cases and control regarding YLK-40 median value (p<0.001) with higher median YLK-40 among cases than control (49.71 versus 37.24) , respectively.

Table (5): Median PASI score distribution among studied cases.

	Cases(n=60)
PASI	15.90
Median (Min-Max)	(1.8-32.1)

Table (5) show that the median PASI score among cases was 15.9 with minimum 1.8 and maximum 32.1.

Table (6): Correlation between PASI and YKL-40 among studied cases

	YKL-40 (ng/ml)	
PASI score	rs=0.564	p<0.001*

rs: Spearman correlation coefficient p:probability
*statistically significant (p < 0.05)

Table (6) show that there is a statistically significant moderate positive correlation between YLK-40 & PASI score (r=0.564 , p <0.001*).

Table (7): Validity of YKL-40 in differentiating cases and control

	YKL-40 (ng/ml)
AUC	0.894
P value	<0.001*
Cut off point	37.96
Sensitivity	93.3%
Specificity	83.3%
PPV	91.8%
NPV	86.2%
Accuracy	90.0%

AUC: Area Under Curve PPV: Positive Predictive value NPV: Negative predictive value

Table (7) show that the area under curve for YKL-40 in differentiating cases and control group was 0.894, the best cut off point with best sensitivity and specificity was 37.96 and total accuracy was 90.0%.

DISCUSSION

Psoriasis is a chronic, immune-mediated, inflammatory, systemic disease of the skin that affects approximately 2-3% of the population worldwide. As such, it has significant implications on physical, psychological and social functioning. It presents as well demarcated dusky red plaques covered with lamellated silvery scales. Although it can be classified as plaque, guttate, pustular and erythrodermic [13], about 80-90% of patients with psoriasis have the plaque form of the disease [14]. One of the principle characters of this disease is excessive proliferation of KCs. However, the precise mechanism of proliferation is not yet fully understood [15]. Up to date, PS has been classified as a complex disease, depending on gene-gene and gene-environment interactions as well as various disturbances in innate and adaptive immunity [16]. In addition, some studies demonstrated that there were some factors involved in development of psoriasis including angiogenesis. Previous studies have demonstrate proliferating endothelial cells in pustular and plaque forms of psoriasis, with a proliferation index of approximately 3% indicating that vascular growth or angiogenesis is an important component in the pathogenethesis of psoriasis [17].

The exact biological functions of YKL-40 are unknown. However, it is suggested that it participate in the physiological and pathological processes such as angiogenesis, mitogenesis and remodeling [8]. Serum levels of chitinase-3-like protein 1(YKL-40) were increased in avariety of inflammatory conditions such as rheumatoid arthritis and chron's disease [10]. In addition YKL-40 was found to play a role in the up regulation of VEGF expression and enhanced angiogenesis. Thus both YKL-40 and VEGF may synergistically promote endothelial cell angiogenesis [18].

The aim of this work was to study the serum level of chitinase -3-like protein1 (YKL-40) in patients with psoriasis in order to assess its possible role in pathogenesis, severity and therapeutic decision of the disease. This study included 60 psoriatic patients and 30 healthy individuals with matched age and sex as a control group. The present study refers to the involvement of YKL-40 in pathogenesis of Ps manifested by its increase in serum of psoriatic patients in comparison to that in control group. These results agreed with studies done by **Imai *et al.*** [10] who compared the serum YKI-40 levels of patients with psoriasis vulgaris and generalized pustular psoriasis with 21 control cases YKL-40 levels were found to be elevated in both psoriasis groups. Moreover, the serum values of YKL-40 in patients with generalized pustular psoriasis were significantly higher than in the psoriasis vulgaris. In addition, **Jensen *et al*.** [19] **and Ahmed *et al*.** [20] reported that serum YKL-40 was higher in psoriatic patients than control and in psoriatic arthritis patients than in psoriasis patients. However, the finding of these studies could not justify the causes of the elevation of this marker, which might be due to inflammation of the diseases, endothelial damage, or the cardiovascular risk factors of the patient such as obesity and smoking. On the other hand, the study of **Ataseven and Kesli** [21] observed that no significant difference in the serum concentration of YKL-40 between psoriatic patients and the control group. **Imai *et al*.** [10] revealed that serum levels of YKL-40 might be a useful biomarker for psoriasis vulgaris and pustular psoriasis and it can reflect the severity of skin lesions in psoriatic patients. Also the study of **Ahmed *et al*.** [20] revealed that PASI

score was important factor influencing YKL-40 levels in all psoriatic patients. This coincide with the result of this study that revealed a positive correlation between serum YKL-40 level and PASI score in psoriatic patients.

Volck *et al.* [22] reported that neutrophil granulocytes share a common progenitor cell with macrophages and neutrophil precursors begin to synthesize YKL-40 at the myelocyte metamyelocyte stage. YKL-40 is stored in the specific granules of neutrophils and released after full activation of the neutrophil. **Imai *et al.*** [10] reported that a major source of serum YKL-40 in pustular psoriasis may be activated neutrophils, because neutrophils strongly express YKL-40 in the epidermis to form spongiform pustules of kogoj. Therefore, YKL-40 may be a useful biomarker which reflects the clinical course and severity of psoriasis.

CONCLUSION

It could be concluded that Chitinase-3-like-protein 1 (YKL-40) may participate in the pathogenesis of psoriasis manifested by its up-regulation in serum of psoriatic patients group in comparison to control group. Chitinase-3-like-protein 1 (YKL-40) can be used as a new marker for evaluation of disease severity and progression in psoriasis. Chitinase-3-like- protein 1 (YKL-40) may open the way for a further therapeutic approach in the treatment of psoriasis.

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