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Comparing the Disease Severity in Iraqi Psoriasis Patients According to Some Immunological and Biological Factors

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Abstract

Psoriasis is a chronic inflammatory skin disease that is closely related to the oxidative stress state of the body. The current study focused on some immunological indicators directly related to inflammation (Procalcitonin, and lysozyme) with the aim of investigating their potential as a prognostic factor for psoriasis. This study included 150 samples, including 90 patients with psoriasis and 40 people who appeared to be healthy, and was conducted from November 2021 to April 2022. The results showed a significant increase in the level of procalcitonin in patients with psoriasis compared to its level in the control group, while it was noted that the increase in the level of the other indicators was not significant, according to the statistical study. It was found that the highest percentage of psoriasis patients are those with excessive weights, and they constitute 37.8 %, and in the second degree they are obese, and they form 35.6 %, and a large percentage 62.2% of the patients have a family history of as a risk factor, and a percentage of 18.9 of the patients are smokers and the same percentage 18.9% of patients are diabetes, while those who suffer from hypertension accounted for 12.2%. All these indicators showed significant differences compared to the control group. It was also found that the value of the disease severity index in hypertensive patients is lower than that in normal pressure psoriasis patients. This result indicates that there is no association between both disorders. Although the increase in lysozyme level in psoriasis patients is not significant when compared to its level in healthy subjects, its level in smoking psoriasis patients was significantly higher than its level in non-smokers psoriasis patients, and this result indicates the role of smoking in raising the level of this inflammatory marker. It was found that the highest level of procalcitonin (457.79 ± 256.75) pg/ml was in patients over 50 years of age, and the lower the age, the lower the level of procalcitonin. This result confirms the relationship between age and severity of inflammation, the older you get, the greater the inflammation, In addition, there are other inflammatory indicators that were not mentioned in this study.

Keywords: Psoriasis, Procalcitonin, Lysozyme.

مقارنة شدة المرض لدى مرضى الصدفية العراقيين حسب العوامل المناعية والبيولوجية

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الخلاصة

الصدفية هي مرض جلدي التهابي مزمن مرتبط بشدة بحالة الإجهاد التأكسدي للجسم. ركزت الدراسة الحالية على بعض المؤشرات المناعية المرتبطة ارتباطًا مباشرًا بالالتهاب وهي Procalcitonin و lysozyme بهدف التحري عن امكانية استخدامها كعامل تنبؤي لمرض الصدفية. اشتملت هذه الدراسة على 150 عينة ، منها 90 مريضاً بالصدفية و 40 شخصاً بدوا بصحة جيدة ، واجريت في المدة من نوفمبر 2021 إلى أبريل 2022 . أظهرت النتائج ارتفاعا معنويا في مستوى البروكلسيتونين لدى مرضى الصدفية بالمقارنة مع مستواه لدى مجموعة السيطرة ، فيما لوحظ أن الزيادة في مستوى المؤشر الآخر لم تكن معنوية بحسب الدراسة الإحصائية. وتبين أن أعلى نسبة من مرضى الصدفية هم أصحاب الأوزان الزائدة ويشكلون 37.8٪ وفي الدرجة الثانية يعانون من السمنة ويشكلون 35.6٪ ونسبة كبيرة 62.2٪ من المرضى لديهم تاريخ عائلي بالإصابة كعامل خطورة ، ونسبة 18.9٪ من المرضى مدخنون ونفس النسبة 18.9 ٪من مرضى السكري ، بينما من يعانون من ارتفاع ضغط الدم يمثلون 12.2٪. كل هذه المؤشرات أظهرت فرقا معنويا مقارنة بمجموعة السيطرة. كما وجد أن قيمة مؤشر شدة المرض لدى مرضى ارتفاع ضغط الدم أقل من تلك في مرضى الصدفية ذات الضغط الطبيعي. تشير هذه النتيجة إلى عدم وجود ارتباط بين كلا الاضطرابين. على الرغم من أن الزيادة في مستوى الليزوزيم لدى مرضى الصدفية ليست كبيرة عند مقارنتها بمستواها في الأصحاء ، إلا أن مستواها في مرضى الصدفية المدخنين كان أعلى بكثير من مستواه لدى مرضى الصدفية غير المدخنين ، وهذه النتيجة تشير إلى دور التدخين في زيادة مستوى المؤشرات الالتهابية. وجد أن أعلى مستوى من البروكالسيتونين (457.79 ± 256.75) بيكوغرام / مل كان لدى المرضى من اللذين تتجاوز اعمارهم الخمسين سنة وكلما قل العمر كلما قل مستوى البروكالسيتونين ، تؤكد هذه النتيجة العلاقة بين العمر وشدة الالتهاب. كلما تقدم العمر ، زاد الالتهاب ،بالإضافة إلى ذلك ، هناك مؤشرات التهابية أخرى لم يتم ذكرها في هذه الدراسة.

1. Introduction

Psoriasis is a chronic autoimmune disease affecting the skin of 0.6-4.8% of the world population [1,2]. The disease is characterized by the proliferation of pro-keratinocyte , T cells and cytokines that have a role in the development and/or maintenance of the disease Type 1 T helper cells have been found to be most common in patients with psoriasis [3]. Keratinocyte hyperproliferation and abnormal cell differentiation, which cause epidermal hyperplasia, are the markers of psoriasis. Histological analysis, psoriasis also displayed significant inflammatory immune cell infiltration and vascular dilatation [4,5]. Several studies have shown the association of inflammatory psoriasis with many pathological conditions, including uveitis and arthritis, and it is a risk factor that causes death as a result of the occurrence of cardiovascular diseases (myocardial infarction / cerebral infarction) caused by inflammation, which is one of the most important diseases associated with psoriasis, according to the statistics of the World Health Organization (WHO) [6], Psoriasis is also associated with inflammation and scaling of the skin. The severity of psoriasis ranges from a few scattered red scaly plaques to involvement in almost the entire surface of the body, which may be gradual It gets worse with age [7].

Procalcitonin (PCT) is a 13 kDa molecular weight protein produced by C cells of the thyroid gland in response to pathogens, It is also a primary peptide of the hormone calcitonin, which appears important in homeostasis within the body. Procalcitonin was first identified by Leonard J. Deftus and Bernard A [8,9,10]. In healthy individuals, its levels in the blood reach less than 0.005 g / l, however, the levels are below the detection threshold for both healthy individuals and patients with a viral infection, this demonstrates that a systemic bacterial infection can be identified using the procalcitonin level [11]. In inflammatory dermatosis, a high discriminating level of procalcitonin may be desirable [12].

Lysozyme is also found in epitheliocytes, including some parts of the rough endoplasmic reticulum of the epithelial cells of the pyloric glands, mucinous granules of the stomach, fundic gland cells, Brunner gland epithelial cells (duodenal glands), and Pan [13,14]. Lysozyme was shown to be mostly expressed by psoriatic keratinocytes, which is consistent with their presence in psoriatic scales [15]. The purpose of this study was to measure the effect of inflammatory stress caused by a variety of factors as measured by Procalcitonin, and Lysozyme. Inflammatory factors (Obesity, family history, smoking, diabetes, and blood pressure) in psoriasis patients, as well as their relationship to disease severity.

2. Material and method

The study included 150 individuals, 90 of them are psoriatic patients who attended Yarmouk Hospital in Baghdad, their ages ranged between 11 and 73 years old, in addition to 60 healthy people. both groups, information regarding age, sex, smoking, family history of disease and chronic diseases, and type of treatment was collected through a questionnaire. Body temperature, body mass index (kg/m2), and Psoriasis Area and Severity Index (PASI) were also measured. sample collected were done by, approximately 6 ml of venous blood was drawn by a sterile syringe, and transferred into a gel tube, centrifuged at 2000-3000 rpm for 20 minutes to induce coagulation and to obtain blood serum, where it is kept in an Eppendorf tube at -20 °C.

The collected serum was used to determine the pro-inflammatory parameters according to the manufacturer's protocol. As indicators of inflammation, Procalcitonin and lysozyme level were estimated using Human Procalcitonin ELISA(China) kits, and Human Lysozyme(LZM)ELISA (China) kits.

3. Statistical Analysis

The data were analysed using the following software, Microsoft Excel, and IBM SPSS V26. The results reported in this study were expressed as mean SD., Z-test was used to compare two proportions. Independent t-tests were used to test between study groups. One-way ANOVA was used to test continuous variables (Severity Index (PASI), lysozyme, procalcitonin) according to age group, and category of BMI. The chi-square test of association was used to describe the immunological and biological factors and the relationship to disease severity of the two study groups. The Pearson correlation evaluates the linear relationship between two continuous variables, and if the categorical variable has two levels, a point-biserial correlation was used. Probability values less than 0.05 were considered significantly different [16].

4. Results and discussion

Table 1 shows the values and levels of indicators that were measured in psoriasis patients compared to the control group, and it was observed that there was a significant increase in both the level of procalcitonin and body mass without other inflammatory indicators, and according to the statistical study, a higher incidence of the disease was observed in patients with weight High as indicated by the results of body mass, while there were no significant differences in body temperature between the two groups.

Table 1: Data of the studied groups and inflammatory markers levels in psoriatic patients compared with healthy controls

Variable	Patient N=90	Control N=57	P-value
Body Temperature (C°)	36.38 ± 1.03	36.64 ± 0.83	0.097 N.S
BMI (Kg/m^2)	28.06 ± 5.69	24.87 ± 3.23	0.001**
Lysozyme (ng/ml)	32.38 ± 27.91	26.16 ± 25.32	0.166 N.S
Procalcitonin (pg/ml)	370.95 ± 180.38	264.29 ± 170.93	0.001**

**** Highly significant (P<0.01) , N.S : non-significant**

Some patients with autoimmune diseases who do not have bacterial infections may have increased serum procalcitonin levels, according to Tamaki *et al.*, [17]. In generalized psoriasis patients, serum procalcitonin levels performed equally well in making a distinction between bacterial infection and non-infection. Procalcitonin has a lesser diagnostic sensitivity than C-reactive protein. However, procalcitonin's specificity outperformed that of the C-reactive protein [18]. Serum procalcitonin levels in Generalized Pustular Psoriasis patients increased slightly in 2018[19]. Patients with psoriasis, especially those requiring systemic therapy, often appear to be overweight [20], moreover, psoriasis has been linked to a variety of chronic metabolites, such as obesity, which appears to be both a risk factor for psoriasis onset and an aggravating factor for disease severity. The World Health Organization has also classified overweight and obesity as a global epidemic [21,22], All these indicators showed a significant difference in Tables 2 and ~~above~~ 6, where the number and percentages of some indicators and characteristics of patients compared with the control group appear. For example, it was found that the highest proportion of patients with psoriasis was overweight, making up 37.8%, and in the second degree obese, making up 35.6% (Table 2), and a significant proportion of patients 62.2% had a family history as a risk factor (Table 3), 18.9 percent of smokers (Table 4) and the same 18.9% of patients have diabetes (Table 5), while those with hypertension account for 12.2% (Table 6) compared with the control group.

Table 2: Mean of BMI in Psoriatic Patients and Controls

BMI	Patient		Control		Total	
	N	%	N	%	N	%
Under-weight	4	4.4	3	5.3	7	4.7
Normal weight	20	22.2	26	47.4	46	30.7
Over-weight	34	37.8	30	43.9	64	42.7
Obese	32	35.6	1	3.5	33	22.0
Total	90	100	60	100	150	100
Chi-Square Test			P-value		0.001**	

**** Highly significant (P<0.01)**

Table 3: Family history in Psoriatic Patients and Controls

Family history	Patient		Control		Total	
	N	%	N	%	N	%
Yes	56	62.2	0	0.0	56	37.3
No	34	37.8	60	100.0	94	62.7
Total	90	100	60	100	150	100
Chi-Square Test			P-value		0.001**	

**** Highly significant (P<0.01)**

Table 4: Percentage of Smokers in Psoriatic Patients and Controls

Smoking	Patient		Control		Total	
	N	%	N	%	N	%
Yes	17	18.9	20	33.3	37	24.7
No	73	81.1	40	64.9	113	75.3
Total	90	100	60	100	150	100
Chi-Square Test			P-value		0.044*	

*** Significant (P<0.05)**

In addition, there is a close association between the severity of obesity and psoriasis severity, as patients with high levels of obesity respond less effectively to systemic psoriasis treatment. Several studies have shown that white adipose tissue is an important site for the production of traditional cytokines such as IL-6 and TNF-α as well as pro-inflammatory molecules including leptin, adiponectin, and resisting. These facts strongly suggest that obesity is a risk factor for the development of psoriasis through inflammatory pathways and that obesity exacerbates pre-existing psoriasis [23].

There is an important association between psoriasis and family history. About 40% of patients with psoriasis have a family history of the disease, which may also affect clinical symptoms [24].

It is well known that people with psoriasis smoke more frequently [25], Smoking also seems to harm the direction of psoriasis naturally, smoking more than 20 cigarettes per day increases the risk of having clinically more severe psoriasis by double [26].

Table (5): Percentage of diabetes in Psoriatic Patients and Controls

Diabetic	Patient		Control		Total	
	N	%	N	%	N	%
Yes	17	18.9	0	0.0	17	11.3
No	73	81.1	60	100	133	88.7
Total	90	100	60	100	147	100
Chi-Square Test			P-value		0.001**	

**** Highly significant (P<0.01)**

Lynch first discovered a link between psoriasis and hyperglycemia in 1967 [27]. Since then, other research has supported the association between psoriasis, hyperglycemia, and insulin

resistance [28,29,30]. Patients with psoriasis exhibit hyperinsulinemia and resistance to insulin. Insulin also, with a clear association between insulin secretion and disease severity positively correlated [31]. Higher insulin levels may result in higher amounts of insulin-like growth factor (IGF) in psoriasis contributing to epidermal hyperproliferation [32].

Table 6: Percentage of Hypertension in Psoriatic Patients and Controls

Hypertension	Patient		Control		Total	
	N	**%**	**N**	**%**	**N**	**%**
Yes	**11**	**12.2**	**0**	**0.0**	**11**	**7.3**
No	**79**	**87.8**	**60**	**100**	**136**	**92.7**
Total	**90**	**100**	**57**	**100**	**147**	**100**
Chi-Square Test			**P-value**		**0.006****	

**** Highly significant (P<0.01)**

Hypertension in patients with psoriasis is now more prevalent when compared to controls, and this has been observed in those studies [33,34,35]. A study of many cases was conducted in a hospital for comparison with controls, and there was a significant increase in the prevalence of essential hypertension in 100 people with psoriasis compared to controls [36].
(Table 7). This result confirms the relationship between age and severity of inflammation. The higher the age, the greater the inflammation

Table 7: Relationship between age categories and Procalcitonin serum level

Age groups (Year)	N	Procalcitonin (pg/ml) Mean ± SD			P-Value¥
< 20	**18**	**267.59**	±	**104.29**	**0.004 ****
20 - 29	**19**	**431.02**	±	**111.71**	
30 - 39	**19**	**403.29**	±	**207.43**	
40 - 49	**19**	**307.91**	±	**133.22**	
≥ 50	**15**	**457.79**	±	**256.75**	

¥: One-way ANOVA was used, **: Highly significant (P<0.01)

In Table 7, the mean minimum value of procalcitonin in psoriasis patients aged less than 20 years was (267.59±104.29) pg/ml, and the highest (457.79 ±256.75) pg/ml was in psoriasis patients over 50 years of age. There appears to be a statistically significant [37], in the procalcitonin concentration difference between the age groups (p = 0.00). Depending on one of the study findings, this may reflect disease severity and patient outlook [38]. Also, this production corresponds to the statistical production of the group of patients according to the age coefficient table 8, which shows that the age range for psoriasis patients is between 11 to 73 years old. The results showed the highest rate of 21.1 % for psoriasis among age groups (20-49 years), which were mostly high in those age groups and are agreed with the results [39,40].

Table 8: Distribution of age categories in Psoriatic Patients and Controls

Age group	Patient		Mean ± SD	P-value
	N	%		
< 20 yr	18	20.0	14.72 ± 2.78	
20 - 29 yr	19	21.1	24.21 ± 2.94	
30 - 39 yr	19	21.1	32.84 ± 3.02	0.001**
40 - 49 yr	19	21.1	43.84 ± 3.22	
≥ 50 yr	15	16.7	59.07 ± 7.87	
Total	90	100		

Psoriasis severity Index is inversely correlated with weight groups. Under and normal-weight groups suffer from increased disease severity compared to other groups. It was found that the lowest value of PASI (9.68) was in obese patients, and the highest value of PASI (20.82) was in normal-weight patients, as shown in Table 9.

Table 9: Relationship between BMI and Psoriasis severity index (PASI)

BMI (Kg/m^2)	N	Psoriasis severity index (PASI) Mean ± SD			P-Value¥
Under-weight	4	20.13	±	16.39	0.018*
Normal-weight	20	20.82	±	15.40	
Over-weight	34	17.07	±	15.07	
Obese	32	9.68	±	8.02	

¥: Independent t-test was used, **: Highly significant (P<0.01)

According to studies, adiponectin has insulin-sensitive and anti-inflammatory properties, which is consistent with our findings. In psoriasis, our study found a weak inverse association between total adiponectin and BMI. Adiponectin generally reduces diabetes and obesity and is negatively correlated with BMI [41,42,43]. where adiponectin levels are positively correlated with PASI and this agrees with our study [44,45]. As Adiponectin has been reported to be a more accurate and sensitive indicator of obesity and the clinical severity of psoriasis [46].

It was found that the value of the disease severity index in hypertensive patients is lower than that in patients with normal pressure psoriasis, as shown in Table 10. This result indicates that there is no association between both disorders.

Table 10: Relationship between Hypertension and Psoriasis severity index (PASI)

Hypertension	N	Psoriasis severity index (PASI) Mean ± SD			P-Value¥
Yes	11	8.69	±	6.31	0.005**
No	79	16.34	±	14.17	

¥: Independent t-test was used, **: Highly significant (P<0.01)

Gisondi *et al* [47] discovered a significant lowering in PASI, the outcome, and chemical levels in the blood, but no correlation was specified between these two parameters. This study aimed to determine the effect of low PASI, high blood pressure, and insulin resistance on patients with psoriasis. The results showed a significant decrease in PASI [48], This agrees with the results of our study in Table (9). While the results obtained indicate the role of smoking in increasing the severity of the disease, as shown in Table 11, it was found that the value of the

coefficient against the disease among smokers' psoriasis patients is higher than its value in non-smokers.

Table 11: Relationship between Smoking and Psoriasis severity index (PASI)

Smoking	N	Psoriasis severity index (PASI) Mean ± SD			P-Value¥
Yes	**17**	**21.85**	**±**	**12.20**	**0.030***
No	**73**	**13.91**	**±**	**13.63**	

¥: Independent t-test was used, **: Highly significant (P<0.01)

The new idea behind psoriasis is oxidative stress, the most important mode of action of tobacco smoke is oxidative stress due to the direct effect of free radicals present in smoke [49]. Smoking increases the risk of developing psoriasis. Direct transport of oxidants and the consequent development of oxidative stress have been implicated in the pathogenesis of smoking-induced psoriasis [50]. Additionally, a significantly marked increase in the PASI score was noticed among smokers compared to non-smokers ($P < 0.001$) [51], also, a significant relationship between smoking duration and the clinical severity of psoriasis has been identified [52].

Although the increase in the level of the lysozyme in patients with psoriasis is not significant when compared to its level in healthy people, according to Table 1, its level in smoking psoriasis patients was significantly higher than its level in non-smokers' psoriasis patients, and this result indicates to the role of smoking in raising the level of this inflammatory marker.

Table 12: Relationship between Smoking and Lysozyme (ng/ml)

Smoking	N	Lysozyme (ng/ml) Mean ± SD			P-Value¥
Yes	**17**	**44.33**	**±**	**37.01**	**0.049***
No	**73**	**29.60**	**±**	**24.84**	

¥: Independent t-test was used, **: Highly significant (P<0.01)

Often found in monocytes and macrophages, lysozyme is an enzyme that can hydrolyze the peptidoglycan of the bacterial cell wall by catalyzing monocytes' muramyl peptides. To produce various cytokines, including IL-1, IL-6, and TNFa, which are also associated with psoriasis [53, 54]. A significant connection between the measured lysozyme biomarkers and tobacco smoke has been found [55].

5. Conclusion

We conclude that procalcitonin, which is one of the indicators of inflammation, is a predictive factor for patients with psoriasis, as well as the relationship of procalcitonin between age and severity of inflammation. Smokers and this lysozyme level indicate the role of smoking in increasing the level of inflammatory markers in patients, in addition to the clear association between oxidative stress and psoriasis patients, which came as positive relationships among all these factors (weight gain, smoking, diabetes, and finally patients with a family history) with psoriasis patients.

6. Ethical Clearance

The committee that was set up by the Department of Biotechnology agreed to perform the experiments in this study. All volunteer patients gave consent to give blood samples. This study was conducted at Yarmouk Hospital in Baghdad under the supervision of doctors at the National Diabetes Center at Al-Mustansiriya University in Baghdad.

7. Cconflict of Iinterest

There is no conflict of interest of any kind between the authors.

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