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Anti-Neutrophil Antibodies (ANCA) Level in Psoriatic Patients with Different Degree of Severity

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Abstract

Psoriasis is a chronic, autoimmune skin disease with cutaneous manifestations; association of several factors including environmental, genetics and immunological abnormalities with psoriasis is documented.

The acronym ANCA (Anti-Neutrophil Cytoplasmic Autoantibodies) is defined by an accumulation of autoantibodies with specificity against different granulocytic, monocyte and probably endothelial cytoplasmic antigens include (elastase, lactoferrin, lysozyme and Cathpsin G), are most commonly found in systemic vasculitis, necrotizing vasculitis and in active generalized wegener's granulomatosis.

The objective of this study is to assess the anti-neutrophil antibody level (ANCA) as inflammatory markers in patients with psoriasis with different degree of severity, correlate the results with the degree of severity and compare the level of these antibodies with those of control group.

This study was conducted from Feb. 2014 to Feb. 2015, blood samples were collected from thirty two persons attending to Al-Karama Teaching Hospital, Baghdad Teaching Hospital and private clinics, sixteen of them having psoriasislabelled as study groups and the rest were free of the disease labelled as control group. The psoriatic patients were classified into three groups according to the degree of severity of the disease as mild (four patients), moderate (four patients) and sever (eight patients), the Psoriasis Area Severity Index (PASI) were used to assess the severity of the disease. Thepatient'sgroup distributed as male (31.2%) and female (62.8%), the serum level of ANCA antibody was measured in thepatient's serum of different degree of severity and in control group by using EnzymeLinked Immunosorbent Assay technique (ELISA) in laboratory of Al-karama Teaching Hospital.

The results proved that the serum levels of ANCA in psoriatic patients were significantly higher than that of control group in all degree of disease severity when ANOVA test used to analyze the data, also the results reported that the level of anti- elastase and ant-lactoferrin were significantly higherin sever degree group of psoriatic patients than mild and moderate degree groups ($p \leq 0.05$)when tested by LSD test, no significant difference was noted between mild and moderate degree groups ($p > 0.05$).

From that we can conclude that autoantibodies against neutrophil antigens are generally associated with inflammatory psoriatic disorder; In addition, the autoantibodies levels were related to the degree of severity of the disease especially antielastase and antilactoferrin.

Keywords: *Psoriasis, Anti-neutrophil Antibody ANCA, Autoimmune disease.*

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تقدير مستوى الاجسام المضادة لخلايا الدم البيضاء العدلة في مرضى الصدفية في درجات مختلفة من شدة المرض

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الخلاصة :

الصدفية هو أحد أمراض المناعة الذاتية التي تصيب الجلد وهناك عدة عوامل ترتبط بظهور المرض منها عوامل بيئية ووراثية ومناعية، أما (ANCA) فهي مختصر لمجموعة الأجسام المضادة الذاتية المنشأ ضد خلايا الدم البيضاء العدلة والتي تتراكم كأضداد ضدالحبيبات المختلفة الموجودة في خلاياالدم البيضاء نوع العدلة وتشمل (إيلاستيز، اللاكتوفيرين، اللايسوزوم والكاثيسين جي)، وقد أثبت وجود هذه الاجسام المضادة أكثر شيوعاً في أمراض التهاب الأوعية الدموية وأمراض المناعة الذاتية المختلفة الاخرى.

الهدف من الدراسة هو تقييم مستوى الاجسام المضادة لكافة انواع الحبيبات ANCA الموجودة في خلايا الدم العدلة وتعتبر من العلامات الالتهابية في مرضى الصدفية وربط مستوى هذه الاضداد مع مستوى شدة المرض ومقارنة مستوياتها في مجموعة المرضى مع مجموعة السيطرة.

أجريت هذه الدراسة للفترة من شهر شباط 2014 الى شهر شباط 2015 وتم اختيار32 شخصاً من مستشفى الكرامة التعليمي ومستشفى بغداد التعليمي والعيادات الخاصة، 16 منهم مصابين بمرض الصدفية ومجموعة أخرى هي مجموعة السيطرة تشمل 16 شخصا غير مصابين بمرض الصدفية. تم تصنيف المرضى الى ثلاثة مجاميع وفقاً لشدة المرض على النحوالتالي: إصابات خفيفة (4 مرضى)، متوسطة الاصابة (4 مرضى) والحالات الشديدة (8 مرضى) وتم إعتماد مؤشرشدة الاصابة للصدفية (PASI) لهذا التصنيف وكانت مجموعة المرضى تتكون من 31.2% ذكور و 62.8% إناث. تم قياس مستوى الاجسام المضادة في مصل المرضى ومجموعة السيطرة باستخدام تقنية الانزيم المرتبط للفحص المناعي ELISA.

أظهرت النتائج ان مستويات المصلية للـ ANCA في مرضى الصدفية كان أعلى من مستواها في مجموعة السيطرة في كل درجة من درجات شدة المرض باستخدام التحليل الاحصائي نوع ANOVA test وبينت النتائج أيضاً أن مستوى الاضداد anti-elastase و anti-lactoferrin كانت أعلى بشكل ملحوظ في شديدي الاصابة مقارنة مع مجموعة المرضى الخفيفي أو متوسطي الاصابة وكان الاختلاف الاحصائي واضح معنويا. وأظهرت النتائج أيضاً بانه لايوجد فرق معنوي إحصائي ملحوظ في مستويات الاجسام المضادة بين مجاميع خفيفة الشدة والمتوسطة ($p > 0.05$).

نستنتج من الدراسة أن الأجسام المضادة ضد مستضدات ANCA بصورة عامة معدلاتها أعلى في المرضى المصابين مقارنة مع مجموعة السيطرة وأيضا هناك صلة بين مستويات الأجسام المضادة وإرتباطها مع شدة المرض خصوصاً مستويات الـ antielastase وantilactoferrin.

الكلمات المفتاحية: الصدفية، أجسام مضادة*ANCA*، أمراض المناعة الذاتية.

Introduction:

Psoriasis is a chronic, proliferative, inflammatory and relapsing skin disease, underlying pathophysiological mechanism of psoriasis was not fully understood until now [1,2], but it is believed to be systemic inflammatory disease, especially T-cell dependent inflammation and autoimmune processes have an important role in its pathogenesis along with a combination of genetic, environmental and immunological factors[3,4]. It happens when skin cell division regulating factors are impaired that causes rapid proliferation of keratinocytes and results in inflame-mation[5,6]. Normally, for the movement of the skin cells from it is origin to skin surface about one month required, in psoriasis; it may take only 3 to 6 days [7, 8].

The etiology of psoriasis (or it is sub forms) is unknown both a defect in growth control mechanisms of keratino-cytes and underlying autoimmune process have been implicated [9, 10].

There are several variations of psoriasis but the most common type is chronic plaque psoriasis that is character-ized by red patches covered by silvery, flaky scales[1, 8].

Severity of psoriasis depends on percentage of body surface area affected and the scorethat used to assess the severity of the disease called PASI score (Psoriasis Area Severity Index). PASI is the most widely used measurement tool for psoriasis to assess the severity of the disease according to body surface area involved, the score started from zero (no

Date of acceptance: 14-6-2015

disease), ≤10%(mild), ≥10-30%(moderate) and ≥30% (sever)[11].

Psoriatic lesions can vary in size from pinpoint to large plaques and can be present as erythematous scaly lesion or pustules, these pustules may be localized persistent or generalized pustular lesion[1,12].

The inflammatory response by generating chemotactic substances, triggers the mobilization and activation of the inflammatory cells[1,8] mainly the neutrophils, which may play a crucial role in the clinical evolution of psoriasis. Their activation includes the release of the granule constituents [13, 14] and a metabolic burst, producing reactive oxygen killing system of phagocytosis[15]. The increase in neutrophils in psoriasis seems to be linked to their activation, considering the observed rise in elastase and lactoferrin[16,17]. Lymphokines produced by activated T cell in psoriatic lesions have a strong influence of T-cells, thus they form a vicious cycle-cell mediated inflammation sustaining loop. Although, the interaction between T-cell mediated immunity and epidermal keratinocytes may well explain the maintenance of background (chronic inflammatory) change diffusely observed throughout psoriatic lesions, characteristic neutrophil accumulation under the stratum corneum can be observed in the high inflamed area [18,19].

Recently, alterations in cytokine production and responsiveness to cytokines have been described which may be causally related to the disease process [12].

Anti-Neutrophil-Cytoplasmic-Antibody (ANCA) is auto-antibodies directed against certain components of granulocytes and these include: anti-elastase, antilactoferrin, antilysozymenand anti-cathpsin G [3].

Elastase is serine protease it occurs mainly inpolymorph nuclear leukocyte (PMN), in macrophages and endothelial cell, the dismantling of proteoglycans by neutrophils is mainly due to elastase proteolysis activity[3].

Lactoferrin is an iron binding protein which occurs in high concentrations in secretions at mucosa surfaces in tears and in milk. Lactoferrin resides in the specific granules of PMN and become exocytose upon PMN activation. Duringactive inflammatory disease, raised serum level of lactoferrin have antimicrobial effect depends on it is iron binding capacity, because most of the bacteria require iron for their own physiological pathway[11,20]. In addition, lactoferrin may also promote neutrophil adhesion and migration, representing a negative feedback modulator to prevent recruitment and activation of WBCs in inflammatory sites, by regulating cytokine release from mononuclear cells [21,22].

Lysozyme is a glycosidase is localized in the azurophilic as well as in specific granules of neutrophils and in extracellular liquid compartment like tears and saliva[11].

Cathepsin G is a group of intracellular proteases mainly found in lysosomes, especially of the spleen, the liver and the kidney, it participates to a great part in the destruction of osteoid tissue as of it is hydrolytic properties. Auto-antibodies against cathepsin G occur mainly in collagenases and other related inflammatory rheumatic disease [3,20, 21].

Materials and Methods:

Studied groups:

Sixteen patients are a known case of psoriasis where the diagnosis confirmed by dermatologists attending to Al-Karama Teaching Hospital, Baghdad Teaching hospital and private clinics for follow up were selected to be the study groups. The psoriatic patient classified to three groups according to PASI as mild (less than 10% of skin surface area involved), moderate (≥10 to 30% of skin surface involved) and sever (more than 30% of skin surface involved). The same number of individuals (free of psoriasis) attending to the same medical centers for other purposes other

Date of acceptance: 14-6-2015

than seeking medical advices for psoriasis were included to the control group.

Sample collection:

Five ml of whole blood was collected from the three groups of psoriatic patients and control group using plastic test tubes, then blood sample centrifuged at 3500rpm for 15 minutes, after that the serum separated and kept at -20 ^{0}C until used for assay.

ELISA for estimation of ANCA:

The ANCA antibodies levels were measured by using the Enzyme Linked Immunosorbent assay (ELISA) according to the manufacturer of IMMUNOCHEM Company.

Procedure of the test:

1- A standard was constituted with standard diluents buffer. Serial diluents of the standard were prepared from original standard.
2- One hundred *Ml* of standard, controls or pre-diluted patients samples was added per well of ELISA micro plate induplicate, then the plate was incubated for 30 minutes at room temperature (20-28) ^{0}C.
3- The contents of the well were discarded and washed three times with 300 *Ml* of washing solution.
4- Onehundred *Ml*of enzyme conjugate was added in to each well and incubated for 15 minutes at room temperature, then washed three times with 300 Ml of washing solution.
5- One hundred *Ml* of TMB substrate solution was added into each well, incubated for 15 minutes at room temperature.
6- One hundred *Ml* of stopping solution was added into each well, incubated for 5 minutes at room temperature.
7- Absorbance was measured at 450 nm by spectrophotometer within 30 minutes.

Statistical analysis:

Data description was performed first. The description of data represented by their mean ,standard deviation and standard error, then the data were analyzed using AVOVA test and LSD (Least Significant Differences), $p<0.05$ was considered to be significant.

Results:

The age group of studied groups ranged from 16 to 53 years, and the mean age of the patients groups is (31±SD14) and of control group is (34±SD11) year. Regarding the distribution of the groups according to the gender, the females were represents 68.8% of patients groups and 62.5% of control group, while the males represent 31.2% of patients groups and 37.5% of control group as seen in table-1.

Table-1: Descriptive criteria of studied groups

Psoriatic patients (mild, moderate and sever)		**control**	
Age(years)			
Mean	Standard Deviation	Mean	Standard Deviation
31	14	34	11
Gender			
F	M	F	M
11(68 .8 %/)	5 (31.2)	10 (62.5%)	6 (37.5%)

The collected data were analyzed by using ANOVA test, the result showed that there was a statistical significant difference among the studied groups regarding anti-elastase antibody ($p=0.01$) as seen in table-2 and fig-1.

On multiple comparisons by LSD test, the results revealed there were statistical significant difference between

Date of acceptance: 14-6-2015

group of sever degree of psoriatic patients from one side and mild, moderate degree and control group from other side and the mean level of anti-elastase of sever degree was significantly higher than that of mild moderate, and control groups. (23.3 U/ml ±12.5SD, 6.1±0.6SD U/ml, 1.6 U/ml ±3SD and 1.9 U/ml±1.6SD) respectively, while no statistical significant difference was noted between mild-moderate, mild-control and moderate-control groups as shown in table-3.

Table-2: Mean value of anti–elastase antibody for studied groups.

Studied Groups	N	Mean	S.D.	95% Confidence Interval for Mean(lower and upper bound)		Min.	Max.	p-value
Sever Degree	8	23.3	12.5	12.8	33.8	10.1	50.0	P = 0.01
Moderate Degree	4	6.1	0.6	5.1	7.1	5.3	6.8	
Mild Degree	4	1.6	3.05	3.2	6.4	0.1	6.2	
Control	16	1.9	1.6	1.1	2.8	0.1	6.2	

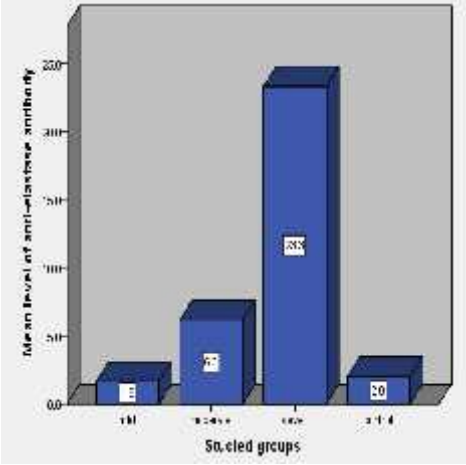

Figure-1: Mean value of Anti-elastase antibody of studied groups.

Table-3: Multiple comparisons between studied groups for anti-elastase antibody level by LSD test.

(I) Degree of severity	(J) Degree of severity	Mean Difference (I-J)	S.E	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Mild	**Moderate**	-4.5	4.5	0.3	-13.9	4.7
	Sever	-21.6	3.9	0.001	-29.7	-13.5
	Control	-.36	3.6	0.9	-7.7	7.03
Moderate	**Mild**	4.5	4.5	0.3	-4.7	13.9
	Sever	-17.1*	3.9	0.001	-25.2	-9.0
	Control	4.2	3.6	0.2	-3.1	11.6
Sever	**Mild**	21.6	3.9	0.001	13.5	29.7
	Moderate	17.1	3.9	0.001	9.0	25.2
	Control	21.3	2.8	0.001	15.5	27.05
Control	**Mild**	.36	3.6	.0.9	-7.03	7.7
	Moderate	-4.2	3.6	0.2	-11.6	3.1
	Sever	-21.3	2.8	0.001	-27.05	-15.5

For lactoferrin antibody level the result showed that there was a statistical significant difference among the studied groups (p=0.01) as shown in table-4 and fig-2, on multiple comparison by LSD test the results revealed there was a statistical

Date of acceptance: 14-6-2015

significant difference between group of sever degree of the psoriatic patients from one side and moderate, mild and control group from other side and the mean level of lactoferrin of sever degree was significantly higher than that of moderate, mild and control groups (10.9 U/ml ±9.6SD, 1.03±0.5SD U/ml, 0.1 U/ml ±0.05 SD and 0.1U/ml±0.07SD) respectively, even the mean value of moderate degree of patients group was higher than that of mild and control groups but no statistical difference was noted between these groups (1.03 U/ml±0.5 SD, 0.1 U/ml ±0.05SD and 0.1 U/ml ± 0.07SD) respectively. No significant difference also noted between mild degree group and control group (0.1 U/ml±0.05SD and 0.1 U/ml±0.07SD) respectively, as seen in table-5.

Table-4: Mean value of anti –lactoferrin antibody in studied groups.

Studied groups	N	Mean	Std. Deviation	95% Confidence Interval for Mean		Min.	Max.	P. value
				Lower Bound	Upper Bound			
Sever Degree	8	10.9	9.6	2.8	19.08	0.4	24.0	0.01 (S)
Moderate Degree	4	1.03	0.5	0.2	1.8	0.3	1.4	
Mild Degree	4	0.1	0.05	0.03	0.1	0.1	0.2	
Control	16	0.1	0.07	0.1	0.2	0.1	0.3	

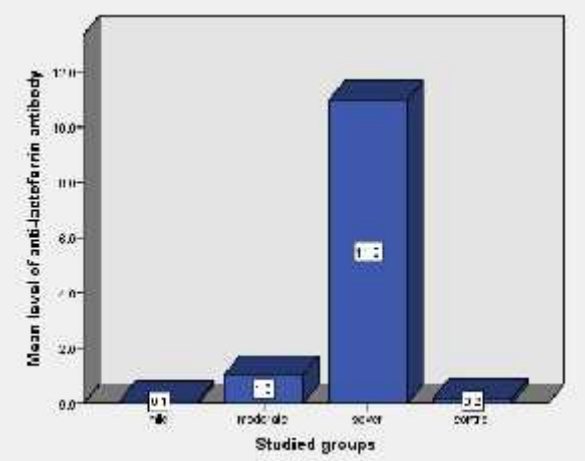

Figure-2: Mean value of Anti-lactofferin antibody of studied groups.

Table-5: Multiple comparisons between studied groups for anti-lactoferrin antibody level by LSD.

(I) Degree of severity	(J) Degree of severity	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Mild	Moderate	-0.91	3.4	0.7	-7.9	6.1
	Sever	-10.8	2.9	0.001	-16.9	-4.7
	Control	-0.07	2.7	0.9	-5.6	5.4
Moderate	Mild	.0.9	3.4	0.7	-6.1	7.9
	Sever	-9.9	2.9	.0.002	-16.0	-3.8
	Control	0.8	2.7	0.7	-4.1	6.3
Sever	Mild	10.8*	2.9	0.001	4.7	16.9
	Moderate	9.9	2.9	0.002	3.8	16.0
	Control	10.7	2.0	0.001	6.4	15.0
Control	Mild	0.07	2.7	0.9	-5.4	5.6
	Moderate	-0.8	2.7	.0.7	-6.3	4.1
	Sever	-10.7	2.0	0.001	-15.0	-6.4

Date of acceptance: 14-6-2015

Table-6 and fig-3 reported significant differences among studied group regarding the mean level of anti-lysozymeantibody (p=0.001), but on multiple comparisons by using LSD test the results revealed a significant difference was noted between control group and groups of patients with different degree of severity, no statistical significant difference was noted between psoriatic patients groups themselves as showed in table-7.

Table-6: The mean value of anti-lysozyme antibody of studied groups.

Study groups	N	Mean	SD	95% Confidence Interval for Mean		Min.	Max.	p-value
				Lower Bound	Upper Bound			
Sever Degree	8	12.8	2.3	10.8	14.7	10.4	16.4	0.001
Moderate Degree	4	10.8	3.6	5.09	16.6	5.5	13.0	
Mild Degree	4	12.3	3.4	6.8	17.7	8.0	16.3	
Control	16	4.6	0.6	4.2	5.01	3.8	5.3	

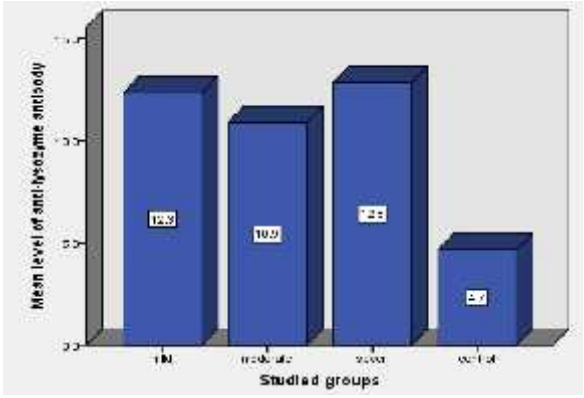

Figure-3: Mean value of Anti-lysozyme antibody of studied groups.

Table-7: Multiple comparisons between studied groups for anti-lysozymeantibodylevel by LSD.

(I) Degree of severity	(J) Degree of severity	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Mild	**Moderate**	1.4	1.4	0.3	-1.5	4.4
	Sever	-0.5	1.2	0.6	-3.1	2.0
	Control	7.6	1.1	0.001	5.2	10.0
Moderate	**Mild**	-1.4	1.4	0.3	-4.4	1.5
	Sever	-1.9	1.2	0.13	-4.5	.6
	Control	6.2	1.1	.0.001	3.8	8.6
Sever	**Mild**	.5	1.2	0.689	-2.0	3.1
	Moderate	1.9	1.2	0.136	-.6	4.5
	Control	8.1	.8	0.001	6.3	10.0
Control	**Mild**	-7.6	1.1	0.001	-10.0	-5.2
	Moderate	-6.2	1.1	.0.001	-8.6	-3.8
	Sever	-8.1	.8	0.001	-10.0	-6.3

Regarding to mean level of anti CathpsinG, the result revealed a statistical significant difference among studied groups by using ANOVA test as seen in Table 8 and fig.4, but on multiple comparisons statically difference was noted between sever degree group and all other groups, the same was noted for control group but no significant difference was noted between mild and moderate degree of psoriatic patients as showed in table-9.

Date of acceptance: 14-6-2015

Table-8: The mean value of anti-cathpsin G antibody of studied groups.

Study variable	N	Mean	SD	95% Confidence Interval for Mean		Min.	Max.	p-value
				Lower Bound	Upper Bound			
Sever Degree	8	31.2	11.5	21.5	40.9	25.0	50.0	0.01
Moderate Degree	4	13.2	0.00	13.2	13.2	13.2	13.2	
Mild Degree	4	10.4	5.05	2.4	18.4	6.2	16.2	
Control	16	2.05	1.6	1.1	2.9	0.2	4.6	

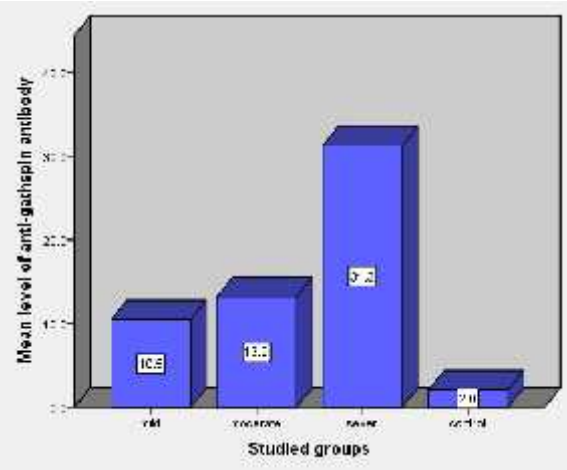

Figure-4: Mean value of Anti-Cathspin G Antibody of studied groups.

Table-9: Multiple comparisons between studied groups for anti-Cahspin G antibody level by LSD test.

(I) Degree of severity	(J) Degree of severity	Mean Difference (I-J)	S.E	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Mild	**Moderate**	-2.7	4.3	0.532	-11.	6.1
	Sever	-20.8	3.7	0.001	-28.5	-13.0
	Control	8.4	3.4	0.02	1.3	15.4
Moderate	**Mild**	2.7	4.3	0532	-6.1	11.6
	Sever	-18.0	3.7	0.001	-25.7	-10.3
	Control	11.1*	3.4	0.003	4.1	18.1
Sever	**Mild**	20.8*	3.7	0.001	13.0	28.5
	Moderate	18.0*	3.7	0.001	10.3	25.7
	Control	29.2*	2.6	0.001	23.7	34.6
Control	**Mild**	-8.4*	3.4	0.021	-15.4	-1.3
	Moderate	-11.1*	3.4	0.003	-18.1	-4.1
	Sever	-29.2*	2.6	.0.001	-34.6	-23.7

Discussion:

Anti-neutrophil antibody (ANCA), are a group of autoantibodies, mainly of IgG type, against antigens in the cytoplasmic of neutrophil granulocyte (the most common type of white blood cell) and monocytes ,they are detected as a blood test in a number of autoimmune disorders[22,23,35], the generation of auto-antibodies are obscure, one possibility may be immunological cross reactivity with microbial super antigens called molecular mimicryby bacteria or other micro-organisms that have the power to stimulate astrong immune response by activation of T-cell or by neutrophil apoptosis [3,21,23]so the pathogenic role of ANCA is still controversial but some ideas support that antibodies have a direct pathological role in the formation of inflammation. MPO (myeloperoxidase) and proteinase-3 PR3

Date of acceptance: 14-6-2015

(predominant specific ANCA molecules) can activate neutrophils and monocytes through their Fc and Fab receptors, which can be enhanced by cytokines which cause neutrophils to display MPO and PR3 on their surface. Activated neutrophil adhere to endothelial cells where degranulation occurs. This releases free oxygen radicals and lytic enzymes resulting in damage to the tissue via the induction of necrosis and apoptosis, furthermore, neutrophils release chemo attractive signaling molecules that recruit more neutrophils to the endo-thelium, acting as a positive feedback loop[25, 26,27]. The increasing level of ANCA in serum of psoriatic patients give evidence that immunological mechanism are involved in the pathogenesis of psoriasis [3,23,24].

The inflammatory response in psoriasis started by generation of chemo-tactic substances and this substances triggers the mobilization and activation of inflammatory cells[25] mainly the neutrophils which playa role in the determining the severity of inflammatory process of psoriasis where their activation lead to the release of the granules constituents[20], this accumulation of neutrophilin psoriasis lesions seem to be result in rise in elastase and lactoferrin more than lysozyme and Cathpsin G granules and this may explain the high level of antielastase and antilactoferrin antibodies than that against of lysozyme and cathpsin G [11,26].

Previous studies mentioned that most anti psoriatic agents interfere in vivo with leukotriene induced by PMN infiltration in human skin, suggesting that this might be one of the anti-psoriatic mechanisms of corticosteroids dithronal and retinoid [27, 28].

Griffiths and Menter et, al.[10,29] reported an imbalance in the protease-anti protease system, with uncontrolled proteolysis by elastase, was proposed to underlie degenerative and derivative disorders [8]. As well as elastase has been found in psoriatic lesions [28] and its activity was associated with scaling and inflammatory activity.

Kuijper et, al.[13] confirmed the high level of elastase and its inhibitors in sever degree of psoriatic patients suggest that it may be seriously involved in spreading of the lesions, besides its crucial role in the worsening of psoriasis, it may provide a marker for monitoring the disease that similar to present finding of increase level of antielastase in sever degree of psoriatic patients, Kuijper and his coworkers [13] explained that one of putative function of PMN elastase is to facilitate migration through connective tissue and basal membranes, towards inflammation foci,in addition they reported that in human skin at least three different high affinity elastase inhibitors can be present simultaneously, either free or complexes alpha -1-antitrypsin (Alpha-1-AT) ,secretory leukocytes inhibitor (SLPI) and SKALP .

The results of this study differ from results reported by Bondt et, al.[31]who has reported that only 4% of psoriatic patients had a positive for ANCA,while in case study done by Quarenghi and his coworkers [32] reported that psoriatic patients have high level of ANCA antibody.

Our finding agree with study of Nikolic et, al.[35]that he was found that p ANCA (perinuclear type) was positive in psoriatic and positive relationship with disease severity.

Similar studies reported that Anti-neutrophil cytoplasmic antibodies found in some autoimmune disease, recognized by their activity with cytoplasmic antigens neutrophils, two groups are recognized :c-ANCA (cytoplasmic type), reacting with proteinase 3, is found in polyangitis and Churg-strauss syndrome, the p-ANCA, reacting with myeloperoxidase is found in Wegener granulomatosis[21,34,35]. We may assume that in psoriasis there is a continuous inflammatory process, underlying a sustained neutrophil activation, an oxidative and proteolysis

stress may turn into a severe form. We considered that it was important to analyses the results and to search for values of risk for worsening of psoriasis. Elastase also may provide a marker for psoriasis and for its worsening, as 95% of patients showed a value above the controls,

Present finding about the circulating autoantibody to neutrophil specific antigen in psoriasis as example of autoimmune disease similar to results of Kutukcular et, al.[21] has been found increase level of autoantibody to neutrophil in other autoimmune disease like systemic lupus erythematosus patients and in rheumatoid arthritis, also study of Terni and Yumanto et, al.[27,33], confirmed present of anti-neutrophil antibody in myasthenia gravis as another example of autoimmune disease.

Therefore, the higher level of ANCA is correlated with severity of the disease especially anti-elastase and antilactoferrin and this parameters can serve as alternative marker for the assessment of severity of psoriasis In addition some other studies showed that some cytokines such as TNF-ALPHA, intrleukin-6, 8 and 17 werehigher in psoriatic patients but not associated with disease severity [30, 31, 34].

In summary, our data showed psoriasis to be an inflammatory condition in which neutrophils seem to play a crucial role by contributing to the development of oxidative and proteolysis stress and found that disease severity which may have indicated by high level of ANCA and significantly related to the severity of thedisease, particularly the serum level of anti-elastase and antilactoferrin.

Conclusions:

The autoantibodies against neutrophil antigens are generally associated with inflammatory psoriatic disorder and the autoantibodies levels were related to the severity of the diseaseespecially antielastase and antilactoferrin.

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