GESDAV

Journal of Investigational Biochemistry

available at www.scopemed.org

Original Research

Adenosine deaminase, malondialdehyde, total antioxidant capacity and eosinophil cationic protein in patients with erythroderma

Amina Hamed Ahmad Alobaidi, Abdulghani Mohamed Alsamarai

Departments of Biochemistry and Medicine, Tikrit University College of Medicine, Tikrit, Iraq

Received: October 05, 2012

Accepted: November 25, 2012

Published Online: December 12, 2012

DOI: 10.5455/jib.20121125074950

Corresponding Author:
Amina Hamed Ahmad Alobaidi,
Tikrit University College of Medicine
aminahamed2006@gmail.com

Key words: Adenosine deaminase, malondialdehyde, total antioxidant capacity, erythroderma, psoriasis.

Abstract

Background: Psoriatic erythroderma may occur in relation to withdrawal of systemic or topica steroids, and its pathogenesis is unclear.
Objective: To investigate serum Adenosine deaminase (ADA) activity in patients with erythroderma and its correlation to malondialdehyde (MDA), total antioxidant capacity (TAC) and eosinophil cationic protein (ECP).
Patients and methods: 26 patients with erythroderma referred to dermatology clinic in Tikr Teaching Hospital were included in the study after giving informed consent. The study wa approved by the ethical committee of Tikrit University College of Medicine. Twenty fiv healthy volunteers, without clinical, laboratory or histological evidence of any disease, wer included in the study as control group. Blood samples were collected and analyzed for seru ADA, MDA, TAC and ECP at the time of inclusion in the study and after complet improvement following methotrexate treatment course.
Results: Mean [±SD] serum ADA activity, MDA, and ECP levels at the time of inclusion in the study were significantly higher than that following methotrexate treatment and control group Serum TAC pretreatment means value was lower than that following treatment, and contr group. Serum ADA levels before treatment was significantly positively correlated with MD serum levels, ECP serum levels and gender. In addition, ADA serum levels were significantl negatively correlated with TAC serum levels. ESR was significantly correlated with ADA MDA, ECP serum levels and negatively with TAC.
Conclusion**:** ADA serum activity and serum levels of MDA,ECP and TAC may be used t predict disease response to treatment and prognosis.

INTRODUCTION

Erythroderma is a rare skin disorder that may be result of many different causes. It is an intense generalized redness of the skin that may be caused by variety of underlying dermatoses, infections, systemic diseases, and drugs [1]. Most of published reports reveal that the majority of patients with erythroderma are diagnosed with psoriasis and spongiotic dermatitis [2]. The preexisting dermatoses form the single most common cause of adult erythroderma [1-9]. Psoriasis and eczema are the most common dermatoses that are progress to erythroderma [1,3,4,8]. Psoriatic erythroderma may occur in relation to withdrawal of systemic or topical steroids, use of systemic medications, such as lithium and antimalarials, phototherapy burns, infections and systemic illness [10]. The pathogenesis of erythroderma is unclear. A reported study suggests a rise in adhesion molecule expression (VCAM-1, ICAM-1, E-selectin, and P-selectin) [11].

Adenosine Deaminase (ADA; EC 3.5.4.4), regulates intracellular and extracellular concentrations of adenosine along with 5'-nucleotidase and adenosine kinase [12]. Activity of ADA has been considered as a marker for non-specific T-cell activation [13-16]. ADA activity increased in some diseases, which characterized T-lymphocytes proliferation and differentiation [17].

Psoriasis is a common skin disorder in Iraq and now it is suggested that the disease can occur due to abnormalities in essential fatty acid metabolism, lymphokine secretion, free radical abnormalities, lipid peroxidation and eicosanoid metabolism [18,19]. Psoriasis in the recent years recognized as systemic diseases, immunometabolic disease that is associated with multiorgan abnormalities [20]. Oxidative stress in patients with psoriasis, which is induced due to overproduction of oxygen metabolites, may overwhelm the antioxidant capacity of the body [21]. Reactive oxygen species production can be indirectly measured by assessing serum MDA [22]. Total antioxidant capacity, a representative of blood antioxidant status, may be reduced in subject with psoriasis, and subsequently the imbalance of oxidant/antioxidant play a role in disease pathogenesis.

Eosinophila was reported as one of the haematological disorders in psoriasis [23, 24], which is a secondary type of eosinophilia. Cationic protein is eosinophil toxin. Which is a potent stimulus of platelet activation and aggregation that can initiate coagulation or inhibition of natural anticoagulant activities [25]? Eosinophilic cationic protein (ECP) when bind to the thrombomodulin, they impair anticoagulant activities, resulting in excessive thrombin generation, which lead to vascular occlusion [26]. Thus peripheral eosinophila in inflammatory diseases, including psoriasis, may represent a problem that may lead to systemic complication.

Methotrexate is a type of drug known as a disease-modifying anti-rheumatic drug. These drugs have the effect of dampening down the underlying disease process, rather than simply treating symptoms. Methotrexate reduces the activity of the immune system (the body's own defense system), so it's always used with care.

There are several studies investigating the role of oxidant/antioxidant systems in the pathogenesis of psoriasis with discordant results [27-29]. To our knowledge this first report that measure these panel in patients with psoriatic erythroderma. A prospective biochemical study performed to investigate serum ADA activity, MDA, Total Antioxidant Capacity (TAC), and ECP in patients with erythroderma.

PATIENTS AND METHODS

Twenty-six patients with erythroderma referring to a dermatology clinic were included in the study after giving informed consent. Erythroderma in all cases were induced due to malpractice of using systemic corticosteroids (All were cases of psoriasis that were treated by systemic corticosteroids). The study was approved by the ethical committee of Tikrit University College of Medicine. A 25 healthy volunteers, without clinical and laboratory evidence of any disease, were included in the study as control group. Blood samples were collected using standard venipuncture technique between 8.00 and 12.00 an m after 12 hour fasting. Serum samples were separated immediately after centrifugation at 4 ^{0}C, 2000xg for 10 minutes and stored at -20 ^{0}C until analysis. For all patients' determination of serum ADA activity, MDA, TAC and Eosinophil Cationic Protein (ECP) were performed at the time of inclusion in the study and after complete improvement induced following methotrexate treatment course. Whole blood collected and used for determination of ESR. The same biomarkers were determined for control individuals.

Determination of serum ADA

Serum total ADA activity was determined at 37 ^{0}C according to the method of Giusti and Galanti [30]. One unit of ADA is defined as the amount of enzyme required to release 1 µmol/min of ammonia from adenosine at standard assay condition.

Determination of serum Malondialdehyde

As index of lipid peroxidation, serum MDA concentration was determined by measuring the thiobarbituric acid reactive substances (TBARS) according to the spectrophotometric method of Janero [31]. The TBARS was determined using OXITEK TBARS Assay kit from Zeptometrix Company. A 100 ul of sodium doedecyl sulfate to the tubes that contain either serum sample or standard and mix thoroughly. Then 2.5 ml of thiobarbituric acid/buffer reagent added down the side of each tube. The tube covered and incubated at 95 ^{o}C for 60 minutes. The tube then removed and cooled to room temperature in an ice bath for 10 minutes. After cooling the samples centrifuged at 3000 rpm for 15 minutes. The supernatant removed from samples for analysis. The absorbance of supernatant measured at 532 nm. Determination of MDA equivalent in µmol/L in samples by interpretation from standard curve.

Determination of serum Total Antioxidant Capacity

The materials used in the determination of TAC in serum include, 2,2-Azobis-(2-amidinopropane) dihydrochloride (ABAP), 6-hydroxyl-2,5,7,8-tetramethylchromane-2-carboxylic acid (Trolox C) were from Sigma- Aldrich.

ABAP was dissolved just before use with a 10 mM phosphate buffer (pH 7.4) at concentration of 5 mg / ml. Crocin was from the association of Saffron producers, Krokos, Kozani, Greece Crocin stock solution prepared in phosphate buffer (10 mM, pH 7.4) at concentration of 20 uM with buffer.

The method for serum TAC determination was as previously described by Kampa M et al [32]. In brief, in each tube 400 µl of crocin and 200 µl of serum sample were pipetted. The reaction was initiated with the addition of 400 µl of pre-warmed (37 ^{0}C) ABAP (5 mg/ml) and crocin bleaching was made by incubating the plate in oven for 60 – 75 minutes. Blanks consist of crocin, serum samples and phosphate buffer (400, 200, 400 µl, respectively) were run in parallel. The absorbance was measured at 450 nm. A standard curve of the water soluble synthetic antioxidant Trolox, prepared prior to use, ranging from 0 – 10 µg/ml was equally assayed under the same conditions.

Determination of serum Eosinophil Cationic Protein

Serum ECP determined by ELISA kit (MBL MESCACUP ECP TEST) from Medical and Biological Laboratories Co, LTD, Japan. This ELISA detects human ECP with a minimum detection limit of 0.125 ng/ml. The test performed according to the instruction of manufacturer. Briefly, in the wells coated with antihuman ECP monoclonal antibody, 100 µl of diluted serum samples (1:5 sample diluent) or standards were added and incubated for 60 minutes at room temperature (20 - 25 ^{0}C). After washing for 4 times, a 100 µl of peroxidase conjugated antihuman ECP polyclonal antibody is added into the wells and incubated for 60 minutes at room temperature. After another 4 times washing, a 100 µl of peroxidase substrate reagent is added to each well and the plate incubated for 10 minutes at room temperature. The added 100 µl of stop solution (0.5 mol/L H_2SO_4) and read the absorbance at 450 nm using a microplate reader. The concentration of ECP is calibrated from a standard curve based on reference standards.

Treatment Schedule

Each patient receive methotrexate orally in a dose of 5 mg/dose (2 tablets) every 12 hours for 3 successive doses. These regimens repeated weekly for 3 successive weeks.

Statistical Analysis

Data were presented as mean (±SD) and 95% confidence interval. Comparison of variables was performed by student's t-test. Two tailed P values < 0.05 were considered significant. Statistical analysis performed using SPSS version 16.0.

RESULTS

The study group of 26 patients with erythroderma was composed of 11 (42.3%) male and 15 (57.7%) female, with a mean age of 39.9 ± 14.6 years, and of range 16-60 years. All the patients are known cases of psoriasis and they developed erythrodema due to misuse of systemic corticosteroids. Clearance of the lesions was obtained with methotrexate treatment regimens (Table 1). Mean [±SD] serum ADA activity at the time of inclusion in the study was significantly (P=0.003) higher [43.42 ± 23.49 U/L] than that following methotrexate treatment [26.15 ± 15.89 U/L]. In addition, the pretreatment mean value was significantly [p=0.02] higher than that of control group [17.93 ± 8.41 U/L]. However, the post-treatment ADA value was higher than that of control individuals.

Table 1. Patients' characteristics

Variable		
Total number		26
Female / male		15 / 11
Age [year]	Range	16 – 60
	Mean ± SD	36.9 ± 14.6
Disease duration [year]		2 – 23
Treatment		Methotrexate

Serum MDA mean value was significantly higher at the time of enrolment in the study [12.52 ± 7.61] as compared to value following treatment [7.54± 5.05, P=0.007] and control [2.37 ± 1.81; P= 0.0001]. Serum TAC pretreatment mean value was 632 [±201], which increased to 857 [±128] following treatment, with significant difference [P=0.0001]. However, the post-treatment mean value was significantly [P=0.0002] lower that than in control [1047 ±207]. ECP serum mean value reduced from 19.73 ± 11.11 µg/l before treatment to 11.61 ± 6.04 µg/l after treatment, with significant difference [P=0.001]. However, the post-treatment serum mean value was higher than that of control group [7.68 ± 5.63 µg/l; P=0.02] (Table 2).

ESR mean value was higher in pre-treatment (24.00±18.21) as compared to post-treatment value (20.34±10.68), however, the difference was not significant. In addition, ESR mean value was significantly (P=0.0005) higher in pre- and post-treatment as compared to control (9.8±5.7) value.

Comparison between male and female for the measured parameters, indicated a significant differences in the pre-treatment mean values for serum ADA (P=0.046) and MDA (P=0.038) only. In addition, non significant differences were achieved for all measured biomarkers following treatment (Table 3).

Table 2. Serum means values of ADA, MDA, TAC, ECP & ESR.

Variable	Mean ± SD [95% Confidence interval]			P value
	Before treatment {A}	After treatment {B}	Control {C}	
ADA (U/L)	43.42±23.49 [34.39-52.45]	26.15±15.89 [20.04-32.26]	17.93±8.41 [14.70-21.16]	A vs. B 0.003 B vs. C 0.02
MDA (µmol/L)	12.52±7.61 [9.59-15.45]	7.54±5.05 [5.60-9.48]	2.37±1.81 [1.67-3.07]	A vs. B 0.007 B vs. C 0.0001
TAC (µmol/L)	632±201 [554-709]	857±128 [807-906]	1047±207 [967-1126]	A vs. B 0.0001 B vs. C 0.0002
ECP (µg/L)	19.73±11.11 [15.46-24.00]	11.61±6.04 [9.29-13.93]	7.68±5.63 [6.08 – 9.68]	A vs. B 0.001 B vs. C 0.02
ESR (mm/h)	24.00 ± 18.21 [17.00 -31.00]	20.34±10.68 [16.23-24.45]	9.80±5.7 [7.72-11.88]	A vs. B 0.38 B vs. C 0.0005

Table 3. Serum mean values of ADA, MDA, TAC, ECP & ESR according to gender.

Variable		Mean ± SD		P value
		Male	Female	
ADA (U/L)	Pre-treatment	32.81±27.98	51.20±8.43	0.046
	Post-treatment	22.72±20.75	28.67±11.29	0.40
MDA (µmol/L)	Pre-treatment	8.96±5.65	15.13±1.70	0.038
	Post-treatment	5.65±3.40	8.93±5.68	0.08
TAC (µmol/L)	Pre-treatment	704±198	580±194	0.12
	Post-treatment	854±142	867±121	0.69
ECP (µg/L)µg/L	Pre-treatment	16.27±10.2	22.27±11.34	0.17
	Post-treatment	10.73±6.75	12.27±5.62	0.54
ESR (mm/h)	Pre-treatment	34.45 ± 20.34	47.53±15.03	0.08
	Post-treatment	17.63±11.78	22.33±9.72	0.29

Table 4. Pearson Correlation Among Variables.

Variable	Sampling time		Age	ADA	MDA	ESR
Age	Pretreatment	r	1.00	-0.27	-0.06	-0.27
		P		NS	NS	NS
	Post-treatment	r	1.00	-0.23	0.02	-0.14
		P		NS	NS	NS
ADA	Pretreatment	r	-0.27	1.00	0.73	0.89
		P	NS		0.000	0.000
	Post-treatment	r	-0.23	1.00	0.65	0.93
		P	NS		0.000	0.000
MDA	Pretreatment	r	-0.06	0.73	1.00	0.69
		P	NS	0.000		0.000
	Post-treatment	r	0.02	0.65	1.00	0.64
		P	NS	0.000		0.000
TAC	Pretreatment	r	0.13	-0.69	-0.81	-0.70
		P	NS	0.000	0.000	0.000
	Post-treatment	r	0.36	-0.55	-0.52	-0.48
		P	NS	0.004	0.007	0.01
ECP	Pretreatment	r	-0.15	0.70	0.38	0.58
		P	NS	0.000	0.05	0.002
	Post-treatment	r	-0.22	0.47	0.08	0.31
		P	NS	0.016	NS	NS
Sex	Pretreatment	r	-0.10	0.39	0.41	0.36
		P	NS	0.04	0.03	NS
	Post-treatment	r	-0.10	0.19	0.33	0.22
		P	NS	NS	NS	NS

Table 5. Oxidative index

Variable	Oxidative index	Patient Oxidative index/ control oxidative index
Pre-treatment	25.77±23.62	11.40
Post- treatment	9.60±8.34	4.25
Control	2.26±0.61	1
P value	0.001	0.001

The correlation among the variables is shown in Table 4. Serum ADA levels before treatment were significantly positively correlated to with MDA serum levels [r=0.73, P=0.000], ECP serum levels [r=0.7, P=0.000], and sex [0.39, P=0.04]. In addition, ADA serum levels were significantly negatively correlated with TAC serum levels [r=-0.69, P=0.000]. Furthermore, ADA serum levels demonstrate a weak negative correlation with age [r=-0.27, P=0.17]. MDA serum levels significantly negatively correlated with TAC [r=-0.81, P=0.000] and positively correlated with sex [r=0.41, P=0.03]. There is a positive correlation between ECP serum levels and MDA, but it not reach a significant levels [r=0.38, P=0.05]. All variables do not demonstrate a significant correlation with age. Table 4

ESR as an established inflammation marker was significantly correlated with ADA (r=0.89, P=0.000), MDA (r=0.69, P=0.000) and ECP (r=-0.58, P=0.002), and negative correlation with TAC (r=-0.70, P=0.000) in the pre-treatment period.

Following treatment with methotrexate all the variables demonstrated the same correlations pattern with the exception of sex correlation with ADA and MDA, correlation of ESR with ECP, which changed from significant to non-significant levels.

The ratio between MDA and TAC [Oxidative index, OD] (Table 5) showed a significant imbalance in patients in pre-treatment (OD=25.77±23.62) and post-treatment (OD=9.60±8.34) when compared with controls (OD=2.26±0.61, P=0.001). Pre-treatment versus post-treatment showed a significant rise in these ratios (P=0.001), as the OI value was eleven fold higher than control value in pre-treatment, and fourfold in post-treatment than in control (Table 5). The individual results (Fig 1) showed that 26 patients (100%) in the pre-treatment group higher than that in control (>3.84), in 20 (76.9%) post-treatment group patients that OI higher than in control (>3.84). The two groups (pre- and post-treatment) were clearly defined for MDA/TAC ratio as compared to control indicating severe inflammatory process in erythroderma.

DISCUSSION

Psoriasis is a chronic inflammatory skin disease characterized by pathological skin lesions because of various exogenous and endogenous factors and associated with a number of biochemical and immunological disturbances [33]. Erythroderma is a rare skin disorders which is mostly due to pre-existing dermatoses [8]. Laboratory findings in the erythroderma patient are usually non-specific [2,34,35].

The present study indicated that mean serum ADA, MDA, ECP and ESR were significantly higher in patients with erythroderma as compared to controls. ADA activity has been found constantly elevated in psoriatic epidermic compared to uninvolved skin [36-38]. Data on serum, lymphocyte and erythrocytes ADA in psoriatic patients are conflicting [12]. Some reported studies found normal ADA activity in peripheral blood lymphocytes [39], serum [40], and erythrocytes [41]. Other studies reported high ADA activities in peripheral blood lymphocytes [42] or plasma [37] or serum [33, 43].

Treatment of erythroderma with methotrexate significantly reduced ADA activities. This finding was consistent with that reported by Vlcek and Mikulikova [42] in psoriatic patients treated with methotrexate. In addition, treatment with PUVA or cyclosporine cause significant decrease in the ADA activities compared to pretreatment values, suggesting a strong relationship between T-cell activation and ADA activity. Most recently, Yildirim et al [43] evaluated patients with psoriasis and observed that mean serum ADA activity reduced significantly following treatment with cyclosporine, entercept, or PUVA.

The serum mean ECP level of erythrodermic patients was found to be significantly higher than that of healthy control. In addition, the mean serum ECP reduced significantly following treatment with methotrexate. Eosinophil cells play active role in many kinds of inflammatory disorders. Recent study [23] indicated a significant eosinophilia in patients with erythrodermic psoriasis. This finding may explain the increase in serum level of ECP in erythrodermic psoriasis as this study indicated. Increased serum ECP seems to be associated with severe form of psoriasis. This finding suggests that the eosinophil have significant roles in the pathogenesis of erythrodermic psoriasis. Although, treatment of erythrodermic

psoriasis with methotrexate reduced serum ECP mean serum value, but still it is higher than that of control. This may suggest that inflammation is present in psoriatic patients even in the absence of skin lesions.

The present study indicated that erythroderma was characterized by reduction in total antioxidant capacity and increased lipid peroxidation. However, treatment with methotrexate leads to reduction in serum MDA and increase in total antioxidant capacity. Furthermore, this study indicated that TAC was significantly negatively correlated with MDA and ADA serum levels. A finding suggests a reduction in antioxidant capacity in patients with erythrodermic psoriasis, associated with increase in lipid peroxidation. In addition, ECP serum levels were significantly correlated to ADA serum levels. Increase in serum ECP was a reflection of eosinophilia which was reported in erythroderma, while serum ADA activity constitutes a marker of cell-mediated immunity [15].

Reported studies [44-46] suggested that ADA deficiency typically causes severe combined immunodeficiency in infants and adults. These studies may let to suggest that presence of high serum level of ADA and ECP may play an important role in the pathogenesis of erythroderma by potentiating of cell-mediated immunity.

In the present study, methotrexate treatment of psoriasis reduced mean serum ADA, ECP and MDA and increased mean serum level of TAC. However, the mean serum level not reaches to that of individual without psoriasis (control). This indicates a significant reduction in inflammatory processes, but not resolved completely, which may suggest that psoriasis is a systemic disease. This suggestion strengthened by post-treatment significant positive correlation of serum levels of ADA, MDA and ECP. Furthermore, significant negative correlation of TAC serum levels with serum ADA and MDA levels was another finding that may strengthen continuity of inflammation in the absence of skin lesions.

In psoriasis, the inflammatory response may be stay balanced or may grow worse, while in erythroderma, the situation is unclear. However, the present study indicated that erythroderma was actually associated with inflammation (Table 2), as shown by the significantly higher levels of inflammatory markers. In post-treatment patient group, these markers were significantly lower than in pre-treatment patient group. Thus erythroderma presented as an inflammatory systemic condition, and its worsening seemed to be linked to precipitating factors.

The inflammatory process by generating a cascade and network of chemotactic substances, trigger the mobilization and activation of the inflammatory cells, namely the eosinophil, which may play a role in the clinical evolution of erythrodermic psoriasis [23, 47]. Their activation includes the release of the granule constituents [48], such as ECP, and ROS production [49]. The increase in eosinophil in erythrodermic psoriasis seems to be linked to their activation, considering the observed rise in serum ECP in erythrodermic psoriasis patients (Table 2). In pre-treatment patients, ECP was about three times the control value and in post-treatment it was significantly higher that value. This suggests that the rise in serum ECP should be influenced by the size of the eosinophil pool, and by its functional activity, shown by secretion of granule contents. This explains the differences in serum mean values between pre-, post-treatment and control groups.

The production of ROS was indirectly assessed the lipid peroxidation level (Tables 2 & 3). We found about a 3 and 6 fold higher value in post-, pre- treatment patients group as that of control value. In addition, lipid peroxidation was significantly higher in pre-treatment than post-treatment patients group, as demonstrated by 2.6 fold of higher OI in pretreatment than in post-treatment group. Furthermore, the OI value was eleven fold higher in pre-treatment as that of control, while it was 4 fold higher in post-treatment as compared to control. The release of eosinophil activation products has to be counterbalanced by well-defined endogenous systems, to reduce or to avoid the enhancement of inflammation. We found in our patients (pre-, post-treatment groups) a significant reduction in TAC and upregulation of MDA and ECP suggesting development of oxidative stress. In post-treatment group, OI value was 4 fold to that of control value, but 11 fold was achieved in pre-treatment group, suggesting TAC depletion.

ESR as established inflammatory marker correlated with high significant value to serum ADA, MDA and inverse correlation to TAC in our patients. This finding suggests that these biomarkers besides its crucial role in the worsening of erythrodermic psoriasis, it may provide markers for monitoring of the disease.

Treatment with methotrexate reduced serum ADA, MDA, ECP, and increased TAC significantly. However, the post-treatment value still significantly higher than that in control, indicating a continuous inflammatory process. This suggests underlying sustained T- lymphocyte, and eosinophil activation and an oxidative stress. Suddenly, this apparently controlled form of psoriasis may turn into a severe form. We considered that it was important to analyze the results and reach for values of risk for worsening of psoriatic erythroderma. We found that ESR, MDA, TAC, ADA and ECP values are meaningful in expression the disease severity, as they were 100%, 100%, 100%,

92.3%, and 84.6% showed values higher than control respectively. Thus we propose this panel as biomarkers of erythrodermic psoriasis and its worsening.

Power analysis was performed to see present effect size of study population on the study findings. The power was 0.96 for ADA, 0.92 for MDA, 0.96 for ECP and 0.99 for TAC. A finding mean that 92% to 99% of studies would be expected to yields a significant effect. The accepted value for power analysis was ≥ 0.80.

In conclusion, ADA serum activity and serum levels of MDA, ECP and TAC may be used to predict disease response to treatment and prognosis. Further studies are needed to strengthen the prognostic significance of the proposed markers for worsening of psoriasis (ADA > 21.6 U/L; MDA > 3.07 µmol/L; TAC < 967 µmol/L; ECP > 9.68 µg/L; OI > 3.84, Table 2). We believe that could be useful in the prognosis of erythrodermic psoriasis, giving clue for disease worsening. This will help physician to start treatment earlier to prevent the disease worsening and it social and psychological impacts [50,51]. In addition, these markers may be used for monitoring treatment response to get rid of aggressive treatment side effects.

ACKNOWLEDGMENT

The authors thank Dr. V. Tsaousis, Medicon Hellas SA, Gerakas, Greece, for gifting the materials used in the determination of TAC in serum.

REFERENCES

1. Botella-Estrada R, Sanmartin O, Oliver V, Febrer I, Aliga A. Erythroderma: A clinicopathological study of 56 cases. Ama Arch Derm Syphilol 1994;130:1503-1507.
2. Okoduwa C, Lambert WC, Schwartz RA, Kubeyinje E, Eitokpah A, Smeeta Sinha, Chen W. Erythroderma: review of a potentially life threatening dermatoses. Indian J Dermatol 2009;54:1-6.
3. Sehgal VN, Srivastava G. Exfoliative dermatitis: A prospective study of 80 patients. Dermatologica 1986;173:278-84.
4. Rym BM, Mourad M, Bechir Z Dalenda E, Faika C, Iadh AM, *et al* . Erythroderma in adults: A report of 80 cases. Int J Dermatol 2005;44:731-5.
5. Akhyani M, Ghodsi ZS, Toosi S, Dabbaghian H. Erythroderma: A clinical study of 97 cases. BMC Dermatol 2005;5:5.
6. Hasan T, Jansen CT. Erythroderma: A follow-up of fifty cases. J Am Acad Dermatol 1983;8:836-40.
7. Leenutaphong V, Kulthanan K, Pohboon C, Suthipinittharn P, Sivayathorn A, Sunthonpalin P. Erythroderma in Thai patients. J Med Assoc Thailand 1999;82:743-8
8. Pal S, Haroon TS. Erythroderma: A clinico-etiologic study of 90 cases. Int J Dermatol 1998;37:104-7.
9. Sigurdsson V, Toonstra J, Hezemans-Boer M, van Vloten WA. Erythroderma: A clinical and follow-up study of 102 patients, with special emphasis on survival. J Am Acad Dermatol 1996;35:53-7
10. Rubins AY, Hartmane IV, Lielbriedis YM, Schwartz RA. Therapeutic options for erythroderma. Cutis 1992;49:424-6.
11. Sigurdsson V, de Vries IJ, Toonstra J, Bihari IC, Thepen T, Bruijnzeel-Koomen CA, *et al* . Expression of VCAM-1, ICAM-1, E-selectin, and P-selectin on endothelium in situ in patients with erythroderma, mycosis fungoides and atopic dermatitis. J Cutan Pathol 2000;27:436-40.
12. Erbagci Z, Erbagci B, Koyluoglu O, Almila Tuncel A. Serum adenosine deaminase activity in monitoring disease activity and response to therapy in severe psoriasis. ACTA MEDICA 2006;49:101-104.
13. Adams A, Harkness RA. Adenosine deaminase activity in thymus and other human tissues. Clin Exp Immunol 1976;26:647-649.
14. Woorhees JJ. Commentary: cyclic adenosine monophosphate regulation of normal and psoriatic epidermis. Arch Dermatol 1982;118:869-874.
15. Bovornkitti S, Pushpakom R, Maranetra N, Nana A, Charoenratanakul S. Adenosine deaminase and lymphocytic populations. Chest 1991;99:789-790.
16. Fontes Baganha M, Pego A, Li ma MA, Gaspar EV, Robalo Cordeiro A. Serum and pleural adenosine deaminase : correlation with lymphocytic populations. Chest 1990;97:605-610.
17. Ozturk ZA, Koklu S, Erol MA, Yilmaz FM, Basar O, Yuksel O, Yilmaz G, Kisacic B, Yuksel I. Serum adenosine deaminase in diagnosis of acute appendicitis. Emerg Med J 2008;25:583-585.
18. Das UN, Vijaykumar K, Madhavi N, Suryaprabha P, Sravankumar G, Ramesh G, et al. Psoriasis current concepts and new approaches to therapy. Med Hypothesis 1992;38:56-62.
19. Popov I, Muller GM, Miehe M, Lewin G, von Baeher R. Relation between the anti-oxidative potential of psoriasis blood plasma in reactivity of granulocytes. Dermatol Monstsschr 1990;176:43-8.
20. Pietrzak A, Michalak-Stoma A, Chodorowska G, Szepietowski JC. Lipid disturbances in psoriasis: an update. Mediators of Inflammation 2010; Article ID 535612, doi:10:1155/2010/535612.
21. Rashmi R, Rao KJ, Basavaraj KH. A comprehensive review of biomarkers in psoriasis. Clin Exper Dermatol 2009;34:658-663.
22. Briganti S, Picardo M. Antioxidant activity, lipid peroxidation and skin diseases. Whats new. J Eur Acad Dermatol Venereol 2003;17:663-669.

23. 23.Mansur AT, Goktay F, Yasar SP. Peripheral blood eosinophilia in association with generalized pustular and erythrodermic psoriasis. J Eur Acad Dermatol Venereol 2008;22:451-455.
24. Sueki H, Nakada T, Iijima M. A case of psoriasis vulgaris with peripheral blood eosinophilia, paralleling the psoriasis area and severity index (PASI) score. Clin Exp Dermatol 2004;29:549-550.
25. Ames PR, Margaglione M, Mackie S, Alves JD. Eosinophilia and thrombophilia in churg strauss syndrome: a clinical and pathogenic overview. Clin Appl Thromb Hemost 2010;16:628-636.
26. Ko JH, Lin JW, Hui RC. Acute pulmonary embolism in a patient with hypereosinophilia and psoriasis. Chang Gung Med J 2011;34(6 suppl):17-23.
27. Gupta M, Chari S, Borkar M, Chandankhede M. Dyslipidemia and oxidative stress in patients with psoriasis. Biomed Res 2011;22:221-224.
28. Ghosh A, Mukhopadhyay S, Kar M. Role of free reactive iron in psoriasis. Indian J Dermatol Venereol Leprol 2008;74:277-278.
29. Baz K, Burak MY, Cimen K, Kokturk A. Oxidant/antioxidant status in patients with psoriasis. Yonsei Med J 2003;44:987-990.
30. Giusti G, Galanti B. Colorometric method. In: Bergmeyer HU, ed. Methods of Enzymatic Analysis. Weinheim: Verlag Chemie, 1984;315-323.
31. Janero D. Malondialdehyde and thiobarbituric acid reactivity as diagnostic indices of lipid peroxidation and peroxidative tissue injury. Free Rad Biol Med 1998;9:515-535.
32. Kampa M, NistikakiA, Tsaousis V, et al. A new automated method for the determination of TAC of human plasma based on crocin bleaching assay. BMC Clinical Pathol 2002; 2:3-21.
33. Hashemi M, Mehrabifar H, Daliri M, Ghavami S. Adenosine deaminase activity, trypsin inhibitory capacity and total antioxidant capacity in psoriasis. J Eur Acad Derm Venereol 2010;24:329-334.
34. Karakayli G, Beckham G, Orengo I, Rosen T. Exfoliative dermatitis. Am Fam Physician 1999;59:625-630.
35. Wilson DC, Jester JD, King LE. Erythroderma and exfoliative dermatitis. Clin Dermatol 1993;11:67-72.
36. Koizumi H, Iizuka H, Aoyagi T, Miura A. adenosine deaminase in human epidermis from healthy and psoriatic subjects. Arch Dermatol Res 1983;275:340-344.
37. Kose K, Utas S, Yazici C, Akdas A, Kelestimur F. Effect of propylthiouracil on adenosine deaminase activity and thyroid function in patients with psoriasis. Br J Dermatol 2001;144:1121-1126.
38. Tikhonov Yu V, Markusheva Li, Toguzov RT. Metabolism of purine compounds in psoriasis. Klin Lab Diagn 1998;3:3-6.
39. Iizuka H, Koizumi H, Kimura T, Moura Y. Adenosine deaminase activity in peripheral lymphocytes of psoriasis and sezary's syndrome. J Dermatol 1980;7:165-169.
40. Koizumi H, Ohkawara A. Adenosine deaminase activity in sera of patients with psoriasis, mycosis fungoides and adult T cell leukemia. Acta Derm Venereol (Stockh) 1992;72:410-412.
41. Beckman G, Beckman L, Cedergren B, Liden S. Red cell enzyme types in psoriasis. Hum Hered 1977;27:408-411.
42. Vlcek F, Mikulikova D. The effect of methotrixate on activity of T-lymphocyte marker enzymes in patients with psoriasis vulgaris. Bratisl Lek Listy 1995;96:137-140.
43. Yildirim FE, Karaduman A, Pinar A, Aksoy Y. CD26/dipeptidyl-peptidase IV and adenosine deaminase serum levels in psoriatic patients treated with cyclosporin, entercept, and psoralen plus ultraviolet A phototherapy. Int J Dermatol 2011;50:948-955.
44. Gilbett ER, Anderson JE, Cohen F, Pollara B, Meuwissen HJ. Adenosine deaminase deficiency in two patients with severely impaired cellular immunity. Lancet 1972;2:1067.
45. Hershfield MS, Mitchell BS. Immunodeficiency diseases caused by adenosine deaminase deficiency and purine nucleoside phosphorylase deficiency In: Scriver CR, Beaudet AL, Sly WS, Valle D (eds.). The Metabolic and Molecular Bases of Inherited Disease. NY, McGraw-Hill, 1995, P 1725.
46. Ozsahim H, Arredondo-Vega FX, Santisteban I, Fuhrer H, Tuchschmid P, Jochum W, et al. Adenosine deaminase deficiency in adults. Blood 1997;89:2849-2855.
47. Mahesar SM, Mahesar H, Khand AA. Quantitative and qualitative changes in leukocytes of psoriatic patients. Pak J Physiol 2011;7:40-43.
48. Kin TY, Park HJ, Kim CW. Eosinophil cationic protein [ECP] level and its correlation with eosinophil number or IgE level in peripheral blood in patients with various skin diseases. J Dermatol Sci 1997;15:89-94.
49. Sannohe S, Adachi T, Hamada K. et al. Upregulated response to chemokines in oxidative metabolism of eosinophil in asthma and allergic rhinitis. Eur Respir J. 2003;21:925-930.
50. Barakin B, Dekoven J. Psychological effect of common skin diseases. Can Fam Physician 2002;48:712-16.
51. Alsamarai AGM, Aljubori AA. Association between stress and skin diseases. MEJIM 2010;3:12-19