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ADENOSINE DEAMINASE: A POTENTIAL BIOMARKER FOR EVALUATING THE SEVERITY OF PSORIASIS

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ABSTRACT

Psoriasis is an immune mediated inflammatory skin disease characterized by epidermal hyper proliferation, impaired differentiation of keratinocytes, excessive angiogenesis and immunological dysfunction. Adenosine deaminase, which catalyses the irreversible hydrolytic deamination of adenosine and deoxyadenosine to inosine and deoxyinosine respectively, plays an important role in the degradation of adenine nucleotide and purine nucleotide salvage pathway metabolism. In psoriasis there is increased purine catabolism, resulting from the marked acceleration of epidermal turn-over. The aim of our study was to evaluate the role of serum adenosine deaminase as a biomarker in severity of psoriasis. The study was performed in 60 clinically diagnosed cases of psoriasis and 60 age and sex matched healthy controls. The patients were scored with psoriasis area and severity index. Our results show increased levels of serum adenosine deaminase in psoriasis patients. This increased levels of serum adenosine deaminase also positively correlated with severity of disease.

KEY WORDS: **Adenosine deaminase, psoriasis, PASI scores, severity.**

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INTRODUCTION

Psoriasis is a common chronic, inflammatory and proliferative disease of skin. Most characteristic skin lesions are red, scaly, sharply demarcated, indurated plaques presenting particularly over extensor surface and scalp. The disease is enormously variable in duration, periodicity of flares and extent[1].Psoriasis is an immunologically mediated disease caused by T-lymphocytes activation that elaborates a Th1 type of immune response. Pro-inflammatory cytokines are involved in the pathogenesis of psoriasis[2,3]. Adenosine deaminase (ADA) activity is a nonspecific marker of the T-cell activation. Cytokines released by both T-cell and keratinocytes mediate keratinocyte proliferation in psoriasis[4].T-cell activation is thought to play an important role in the pathogenesis of psoriasis. ADA activity is elevated in psoriatic epidermis compared to uninvolved skin, possibly due to an increase in nucleic acid metabolism of the hyperproliferatig epidermis of psoriasis[5].Hence this study was carried out to evaluate the role of adenosine deaminase as a biomarker in severity of psoriasis. We also observed the correlation between these levels and the severity of the psoriasis.

MATERIALS AND METHODS

A case control study was conducted to estimate the levels of serum adenosine deaminase. In this study, sixty clinically diagnosed psoriasis patients are recruited from department of Dermatology, C.G. Hospital and Bapuji Hospital attached to J.J.M. Medical College, Davangere (Karnataka) from April 2013 to March 2014. Diagnosis of psoriasis was based on clinical and histo-pathological examination. Sixty controls are selected from a healthy population of Davangere. Psoriasis patients are divided into three groups mild, moderate and severe psoriasis based on Psoriasis Area Severity Index (PASI) score. Psoriasis patients PASI score with 1.0 to 7.9 grouped into mild psoriasis, with 8.0 to 14.9 in moderate psoriasis and 15.0 or more than 15.0 included into severe psoriasis. Each group consisted of 20 patients. Each gave a written consent and this study was approved by the ethical and research committee of J.J.M Medical College, Davangere to use human subjects in the research study. The patients and controls were voluntarily participated in the study. The subjects with a history of any co-existing inflammatory skin disorders, autoimmune disorders like systemic lupus erythematous, rheumatic arthritis, any malignancy, diabetes mellitus, hypertension, cardiovascular disorders, chronic renal disease, heavy smoking and chronic alcoholics, deep fungal or gonococcal infection, pregnant and lactating women were excluded from study. Patients also taking systemic or topical medication and any phototherapy for at least two months were also excluded from study. Under aseptic precaution 5 ml of fasting blood sample was collected in plane bulb and serum was separated after clot retraction. Serum adenosine deaminase was estimated by colorimetric method of Giuseppe Giusti and Bruno Galanti[6]. The statistical analysis was performed using SPSS version 16. In this study to evaluate the difference between the cases and control, we used student's t test. Multiple group comparison was done by one way ANOVA followed by Tukey's Post Hoc test. Results were expressed as mean± SD. A p-value of 0.05 or less was considered as statistically significant.

Table 1
Showing age and sex-wise distribution of controls and cases. Psoriasis cases further divide into three groups based on PASI score

Variables	Controls	Psoriasis Cases			p value Controls v/s Cases
		Mild	Moderate	Severe	
Male (No.)	36	12	12	12	>0.05 NS
Female (No.)	24	8	8	8	>0.05 NS
Age in years (Mean ± SD)	41.9 ± 9.1	42.6± 8.7	42.7 ±8.76	39.7 ±10.6	>0.05 NS
PASI score (Mean ± SD)	-	5.8 ± 1.4	10.8 ±1.89	16.9 ± 1.4	<0.001HS

p value < 0.05 highly significant, > 0.05 not significant

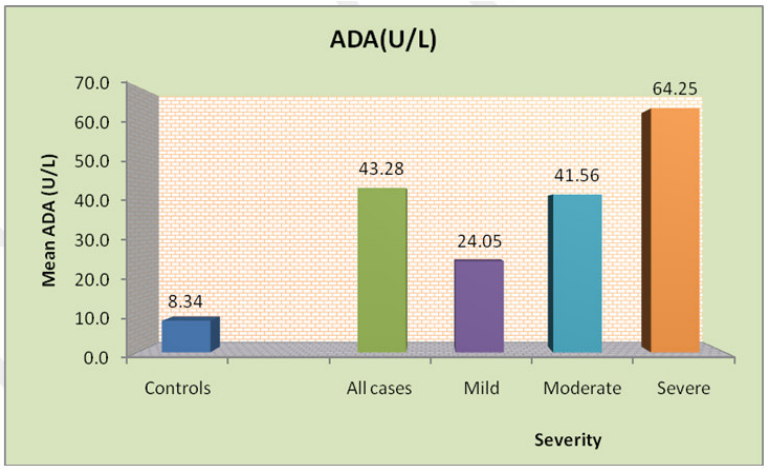
RESULTS

The mean levels of serum ADA are 8.34 ± 3.46 U/L and 43.28 ± 18.47 U/L in controls and psoriasis cases respectively. The statistical analysis by student's t-test shows that serum levels of ADA significantly increased in psoriasis when compared to healthy controls (p<0.001). These levels also increased in different severity groups.

Table 2
Serum ADA levels in controls and different severity groups of psoriasis

Variable	Controls Mean ±SD	Cases (Mean±SD)			Controls / Cases		
		Mild	Moderate	Severe	Mean Diff.	t value	p value
ADA (U/L)	8.34 ±3.46	24.05 ±5.67	41.56 ± 5.29	64.25 ±12.01	34.94	14.10	<0.001

Graph 1
Serum ADA levels in controls and different severity groups of psoriasis



The mean levels of serum of ADA are significantly (p<0.001) increased in subjects with psoriasis (43.28±18.47 U/L) as compared to normal healthy controls (8.34±3.46 U/L). The statistical analysis by one way ANOVA followed by Tukey's Post hoc test shows the comparison of levels of serum ADA in different severity groups of psoriasis. Statistical analysis evaluate the mean levels of serum ADA are successively increased in subjects from mild group of psoriasis (24.05±5.67U/L) to moderate group (41.56 ± 5.29 U/L)and moderate group of psoriasis to severe group of psoriasis (64.25±12.01U/L) significantly (p<0.001).A difference between mild and moderate groups of psoriasis (17.52), between mild and severe psoriasis (40.2), and between moderate and severe psoriasis (22.69) are also obtained which was highly significant (p value <0.001).

Table 3
Comparison of serum ADA levels in different groups with relation to severity of psoriasis.

Groups			ADA(U/L)
1.Mild			24.05±5.67
2. Moderate			41.56 ± 5.29
3. Severe			64.25±12.01
ANOVA	F value		119.25
	p value		<0.001
Difference between groups (p values)	1 v/s 2	Mean Diff	17.52
		p value	<0.001
	1 v/s 3	Mean Diff	40.2
		p value	<0.001
	2 v/s 3	Mean Diff	22.69
		p value	<0.001

One way ANOVA followed by Tukey's Post hoc test.

DISCUSSION

Psoriasis is currently considered as an immunological disorder because of its associations with certain human leukocyte-associated antigens, the presence of activated T lymphocytes in lesions, and good responses to immunosuppressive therapies[7].Psoriasis is a chronic inflammatory skin disease associated with a number of biochemical disturbances. Adenosine deaminase catalyses the irreversible hydrolytic deamination of adenosine and deoxyadenosine to inosine and deoxyinosine respectively[8].Adenosine deaminase activity is elevated in psoriatic epidermis compared to uninvolved skin, possibly due to an increase in nucleic acid metabolism of the hyperproliferative epidermis of psoriasis patients[9]. In this study the mean levels of serum adenosine deaminase in psoriasis patients (43.28±18.47 U/L) were significantly (p<0.001) higher as compared to normal healthy controls (8.34±3.46 U/L). These findings are in accordance with the studies of Gul Bukulmezet al.[10], Erbagei Z et.al[11], Hashemi M et al[12]. These researchers found elevated levels of serum adenosine deaminase in psoriasis subjects as compared to healthy controls. T-cell activation has been implicated in pathogenesis of psoriasis and adenosine deaminase activity has been considered as a marker of T-cell activation[13]. Ozgur H el demonstrates the increased serum level of adenosine deaminase[14]. This study report increased adenosine deaminase activity in diseases with T cell activation. The present study shows a significant increase in levels of serum adenosine deaminase in subjects of severe psoriasis (64.25±12.01U/L) as compared to mild (24.05±5.67U/L) and moderate (41.56 ± 5.29 U/L) subjects of psoriasis. A difference between mild and moderate (17.52), between mild and severe (40.2), and between moderate and severe (22.69) were also obtained which is highly significant (p value <0.001).This difference is reflecting that severity of disease is increasing from mild to moderate and moderate to severe group of psoriasis. The findings of increased serum adenosine deaminase levels in different severity groups in this study is in accordance with the research work of Gul Bukulmez et al[10], Zulal Erbagci et al[11], and Hashemi M et al[12]. Koizumi Het al[13]demonstrate that increased serum activity of adenosine deaminase is correlated with severity of psoriasis and extensive involvement of psoriatic lesions. It reflects the involvement of T-cell activation in the pathogenesis of psoriasis. In present study serum adenosine deaminase is elevated in different groups of severity of psoriasis. Findings of the present study are in accordance with this study. The increased adenosine deaminase activity in the psoriasis affected epidermis may reflect the accelerated salvage pathway of the nucleic acid metabolism probably associated with the hyperproliferative condition of the psoriatic epidermis[15].A study conducted by Yıldırım FE, Karaduman A, Pinar A, Aksoy Y[16] showed significant changes in levels of serum ADA in psoriasis patients. They suggest that ADA may be a useful marker

indicating disease activity and T-cell activation. A study by Saini A Sand Veena G S[17] revealed the significant high adenosine deaminase activity in psoriasis patients as compare to healthy controls. The result of our present study is consistent with the above findings.

CONCLUSION

Psoriasis is an immune mediated inflammatory skin disease characterized by epidermal hyper proliferation, impaired differentiation of keratinocytes, excessive angiogenesis and immunological dysfunction. The exact aetiology of psoriasis is still unknown. Adenosine deaminase activity is regarded as a nonspecific marker of T cell activation. Our findings support the hypothesis that higher levels of serum ADA in psoriasis patients were positively correlated to the severity of the disease. Important points to consider before using adenosine deaminase as biomarkers of psoriasis are the possible influence of environmental, immunological and genetic factors. Finally, we also feel need of further elucidation in role of adenosine deaminase as biomarker of disease severity in psoriasis. At last our research work will be helpful in making novel strategies for diagnosis, treatment and prognosis of psoriasis.

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