"Role Of Serum Adenosine Deaminase Activity In Predicting Disease Severity In Psoriasis Patients"

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ABSTRACT

BACKGROUND: Psoriasis is a group of common, chronic, inflammatory and proliferative conditions of the skin, associated with systemic manifestations in many organ systems.

AIM: To assess the role of serum adenosine deaminase activity in predicting disease severity in psoriasis patients.

MATERIAL & METHODS: This was a hospital based cross-sectional study carried out in the Department of Biochemistry, at Assam Medical College & Hospital, Dibrugarh, Assam, India for a period of 12 months i.e,1st April 2023 to 31st March 2024. The total sample size was 80 which include all newly diagnosed cases of psoriasis attended OPD and IPD of the hospital. The severity of the disease was scored according to Psoriasis Area and Severity Index (PASI).

RESULTS: Out of the total 80 blood samples collected from the psoriasis patients, maximum number of patients were observed from the age group of 30-49(63.75%) and least were found in theage group of 50-60 (15%). The frequency of maleswas higher than that of females, 70% and 30% respectively. Linear regression showed that Serum ADA activity has a positive correlation with disease severity ($r=0.9783$) and statistically significant ($p<0.0001$).

CONCLUSION: In the present study, we concluded that for the purpose of anticipating the severity of psoriasis and monitoring the effectiveness of treatment, serum adenosine deaminase activity can be suggested as a potentially useful biomarker.

KEYWORDS: Serum adenosine deaminase, Psoriasis, PASI, OPD, IPD, inflammation.

INTRODUCTION

Psoriasis is a group of common, chronic, inflammatory and proliferative conditions of the skin, associated with systemic manifestations in many organ systems [1.]World Health Organization (WHO) considered psoriasis as a global health problem [2]. In India the prevalence of psoriasis ranges from 0.4-2.8% [3]. The reported prevalence of psoriasis in countries ranges between 0.09% and 11.4% [4] making psoriasis a serious global problem. PASI is recommended as the current gold standard for assessing the severity of psoriasis and for clinical trials [5, 6,7].

ADA is an enzyme that catabolizes purine nucleotides [8]. It is involved in the hydrolytic deamination of adenosine and 2′-deoxyadenosine to inosine and 2′-deoxyinosine, respectively.

The role of ADA in function and maturation of lymphoid cells, especially T-cell lineage, and its altered status in diseases with immunological disturbances have proven to be very crucial and informative [9].

ADA regulates the plasma adenosine level, which is directly or indirectly involved in inflammatory molecules and cytokine production. The ambiguous nature of ADA gives insight into its involvement in various disorders [10].
The comorbidities of psoriasis included hypertension (1.1% to 27.8%), diabetes mellitus (DM) (7.0% to 13.9%), cardiovascular diseases (4.2% to 8.1%), and tonsillitis (3.5% to 5.4%) [**11**,12,13]. Psoriasis is associated with obesity [14,15,16] and excess adipose tissue may contribute to dyslipidemia. The moderate to severe psoriasis is associated with depression, suicide and rare lymphoma [17]. Patients with psoriasis have a higher prevalence of dyslipidemia, which is likely to increase with the severity of psoriasis [18,19,20,21].
Psoriasis is a chronic skin disorder, with extensive systemic involvement of an unknown etiology. However, the most accepted hypothesis is that it has an immunological involvement due to its association with certain human leukocyte-associated antigens, presence of activated T lymphocytes in lesions, and its response to immunosuppressive therapies [22].
However, this could be due to increased nucleic acid catabolism associated with the hyperproliferative status of epidermis in psoriasis patients. Therefore, the importance of serum ADA may play a significant role in determining the pathogenesis of psoriasis. Therefore, the present study was undertaken to study the role of serum adenosine deaminase activity in predicting disease severity in psoriasis patients.

MATERIAL & METHODS

This was a 1year (From April 01/04/2023 – 31/03/2024) hospital based cross-sectional study conducted in Department of Biochemistry, Assam Medical college & Hospital Dibrugarh, Assam, India. A total 80 blood samples were collected from newly diagnosed psoriasis patients attending both IPD/OPD of the same hospital.
Psoriasis Area and Severity Index (PASI) is the most widely used tool for the measurement of severity of psoriasis. PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease). PASI less than 10 considered as mild Psoriasis and PASI greater than 10 considered as moderate to severe Psoriasis. The body is divided into four sections (head (H) (10% of a person's skin); arms (A) (20%); trunk (T) (30%); legs (L) (40%)). Each of these areas is scored by itself, and then the four scores are combined into the final PASI. For each section, the percent of area of skin involved, is estimated and then transformed into a grade from 0 to6:0% of involved area-grade: 0,< 10% of involved area- grade:1,10-29% of involved area- grade:2,30- 49% of involved area, grade:3,50-69% of involved area-grade:4,70-89% of involved area-grade:5,90- 100% of involved area-grade: 6 Within each area, the severity is estimated by three clinical signs: erythema (redness), induration (thickness) and desquamation (scaling). Severity parameters are measured on a scale of 0 to 4, from none to maximum. The sum ofall three severity parameters is then calculated for each section of skin, multiplied by the area score forthat area and multiplied by weight of respectivesection (0.1 for head, 0.2 for arms, 0.3 for body and0.4 for legs) [23].

Inclusion criteria:
Patients of both genders, aged 18-60 years, newly diagnosed cases of psoriasis were included.

Exclusion criteria:
- Patients with H/O Gout, any Malignancy, Diabetes Mellitus, Hypertension, Tuberculosis, Renal Disorder, Autoimmune disorders were excluded from the study.
- Pregnant and Lactating women.
- Patients not willing to give informed consent.

Ethical clearance: Ethical Clearance was duly obtained from the Institutional Ethics Committee

(Human) of Assam Medical College and Hospital, Dibrugarh [SL No. 157].
Sample collection: The written and informed consent of the participants were taken prior to the study for doing their General Examination, Respiratory Examination, Cardiovascular Examination and Central Nervous Examination. A 5ml of blood sample was collected under all aseptic conditions from patients from antecubital vein using a standard venipuncture technique using a sterile empty vial.

Sample Processing: The sample collected was then allowed to clot.After being clotted, the sample was allowed to centrifuge at 3500 rpm for 10 mins for separation of the serum. After that the collected serum was extracted using micropipette and collected in separate aliquots to be further studied for the required biochemical parameters. The serum sample was processed as early as possible. In case where delay was inevitable, the serum was refrigerated at (2-8℃).

Estimation of Serum ADA level:
Analytical procedure:

METHODS:

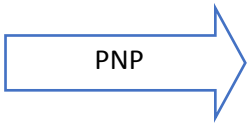
1. BY ENZYMATIC –COLORIMETRIC
2. KINETIC.

NORMAL SERUM ADA REFERENCE RANGE: 0-15 U/L.
Microlab 300 Semi Autoanalyzer was used in the present study.

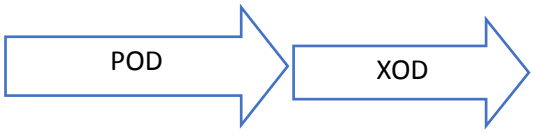
PRINCIPLE: [24]
1. The ADA assay is based on the enzymatic deamination of adenosine to inosine which is converted to hypoxanthine by purine nucleoside phosphorylase (PNP).
2. Hypoxanthine is then converted to uric acid and hydrogen peroxide (H2O2) by xanthine oxidase (XOD).
3. H2O2 is further reacted with N-Ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline (EHSPT) and 4-aminoantipyrine (4-AA) in the presence of peroxidase(POD) to generate quinone dye which is monitored in a kinetic manner.

- **The entire enzymatic reaction scheme is shown below.**

Adenosine + H2O Inosine + NH3 Inosine +NH3



Inosine + Pi Hypoxanthine + Ribose-1-Phosphate



Hypoxanthine + H2O +O2 Uric Acid +H2O2

H_2O_2 + 4-AA + EHSPT H_2O + Quinone dye

One unit of ADA is defined as the amount of ADA that generates one µ mole of inosine from adenosine per min at 37℃.

NORMAL SERUM ADA REFERENCE RANGE: 0-15 U/L.

MILD SERUM ADA RANGE: **16-25 U/L**

MODERATE SERUM ADA RANGE: **26-35 U/L.**

SEVERE SERUM ADA RANGE: **≥35U/L.**

Fig 1: Microlab 300 Semi Autoanalyzer Fig 2: Adazyme^{TM}-LS Reagent

STATISTICAL ANALYSIS:

Qualitative Data was presented as Frequency and Percentage (%).Quantitative Data was presented as Mean ± SD.For Qualitative Data, statistical significance was tested using Chi-Square Test. For Quantitative Data, statistical significance was tested using ANOVA followed by t- Test. The p-value of <0.05 was considered as statistically significant. Statistical Analysis was done using SPSS version 20/MicrosoftExcel sheet.

RESULTS

In the present study out of newly diagnosed 80 Psoriasis patients, 51 of them were belongs to age group of 30-49 (63.75%) while 21.25% and 15%were from the age group of 18-29 and 50-60 respectively. As shown in Table 1.

Table 1: Agewise distribution of Psoriasis patients.

Age Group (in years)	Number of Psoriasis Cases (n)	Percentage (%)
18-29	17	21.25
30-49	51	63.75
50-60	12	15

In this table, it was observed that, 63.75% of patients were belong to age group 30-49 while only 15 % of cases were belong to age group 50-60.

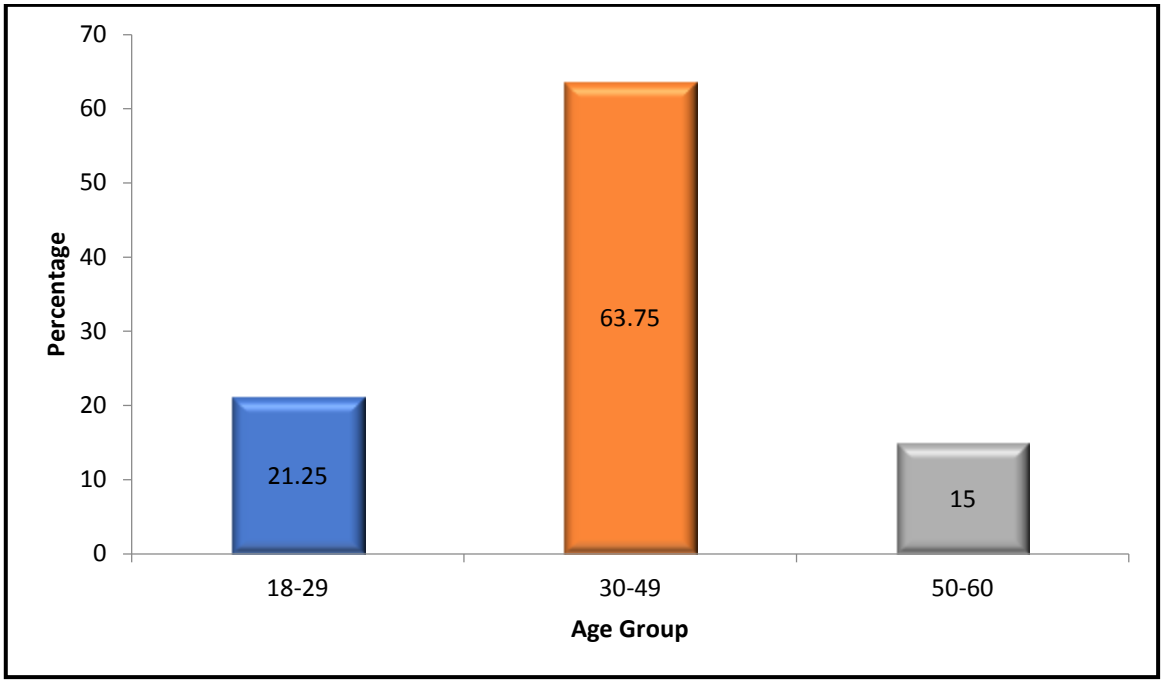


Fig-1: Graphical representation of Agewise distribution of Psoriasis patients.

Among two different variables, Average mean of PASI and age was 12.46 and 37.5 respectively. as shown in Table 2 and Fig-2.

Table 2: Average mean of Age and PASI score.

VARIABLES	Mean	SD
Age in years	37.54	10.27
PASI	12.46	4.96

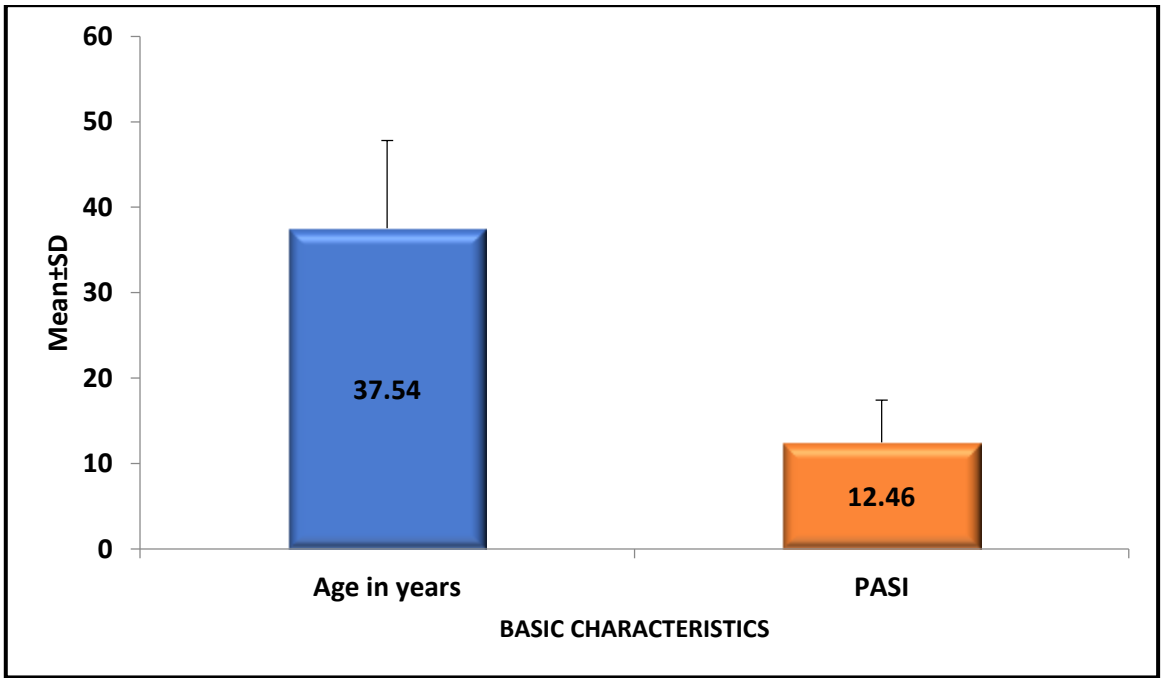


Fig-2: Graphical Representation of the Average mean of Age and PASI score.

The frequency of male patients was higher than that of female psoriasis patients which include, 70% and 30 % respectively. As shown in Table 3 and Fig-3.

Table 3: Gender wise distribution.

Gender	Number (n)	Percentage(%)
Male	56	70.00
Female	24	30.00

In this table, it was observed that,56(70%) were males and 24(30%) were females.

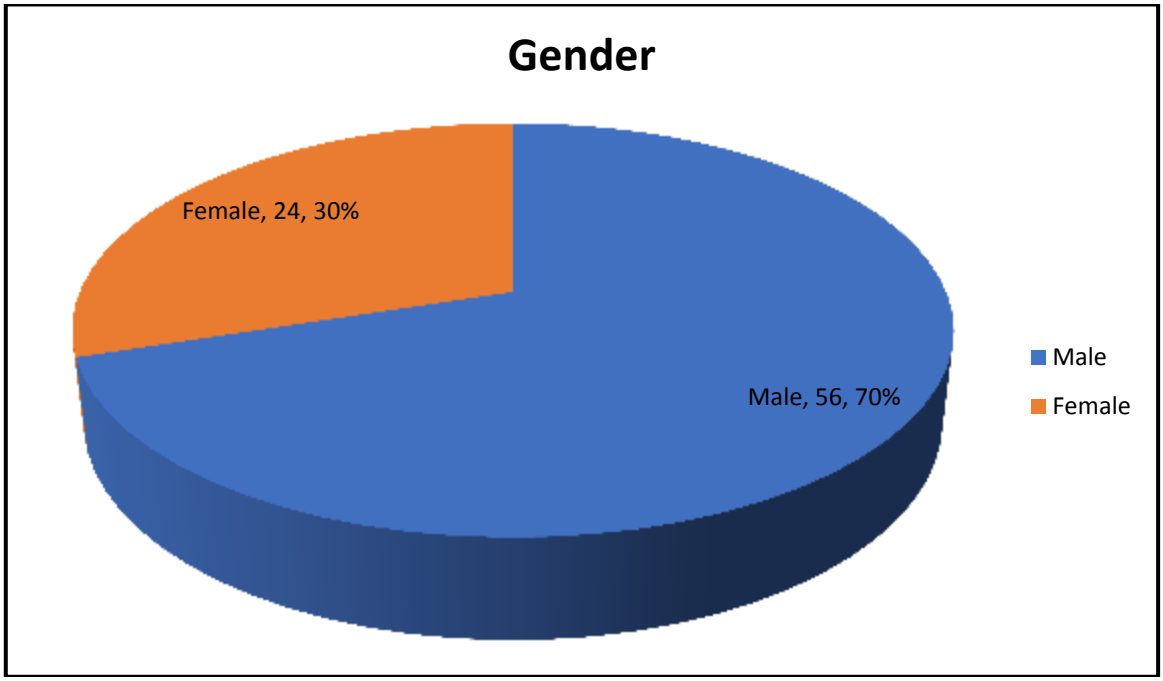


Fig-3: GENDER WISE DISTRIBUTION.

The mean ADA level among all the psoriasis patients were 23.95 ± 5.07 (p Value<0.0001) as shown in Table 4 and Fig-4.

Table 4: ADA level in Psoriasis patients.

PARAMETERS	PSORIASIS PATIENTS MEAN ± SD	r-value	p-VALUE
ADA (U/L)	23.95 ± 5.07	0.9783	<0.0001

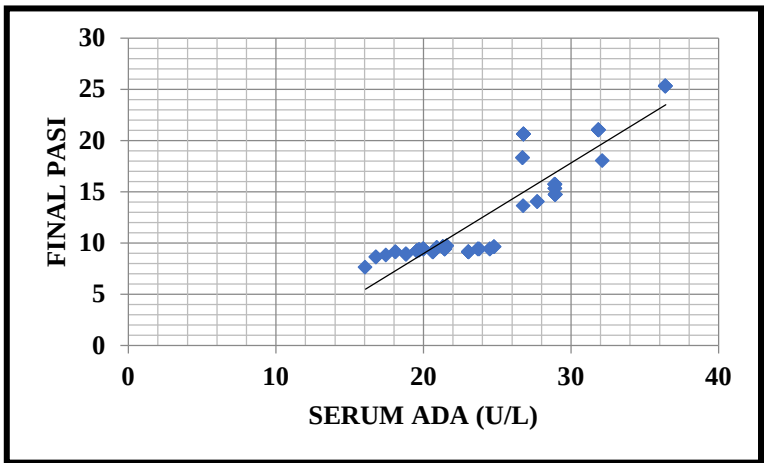


Fig-4: Correlation of serum ADA with final PASI.

The mild, moderate and severe PASI score according to different age group was given in Table 5. In Table 5, it was observed thatPASI score was found maximum in the mild to moderate casesin the age group 30-49, the mild, moderate and severe PASI score was36.25%, 12.5% and 15%

respectivelyfollowed by18-29 yearsand least in the age group of 50-60 years,shown in Table 5 and Fig-5.

Table 5: Age wise distribution according to PASI.[25]

PASI	Age Group(in years)						p-value
	18-29		30-49		50-60		
MILD CASES	15	18.75	29	36.25	8	10	0.0341
MODERATE CASES	2	2.5	10	12.5	4	5	
SEVERECASES	0	0	12	15	0	0	

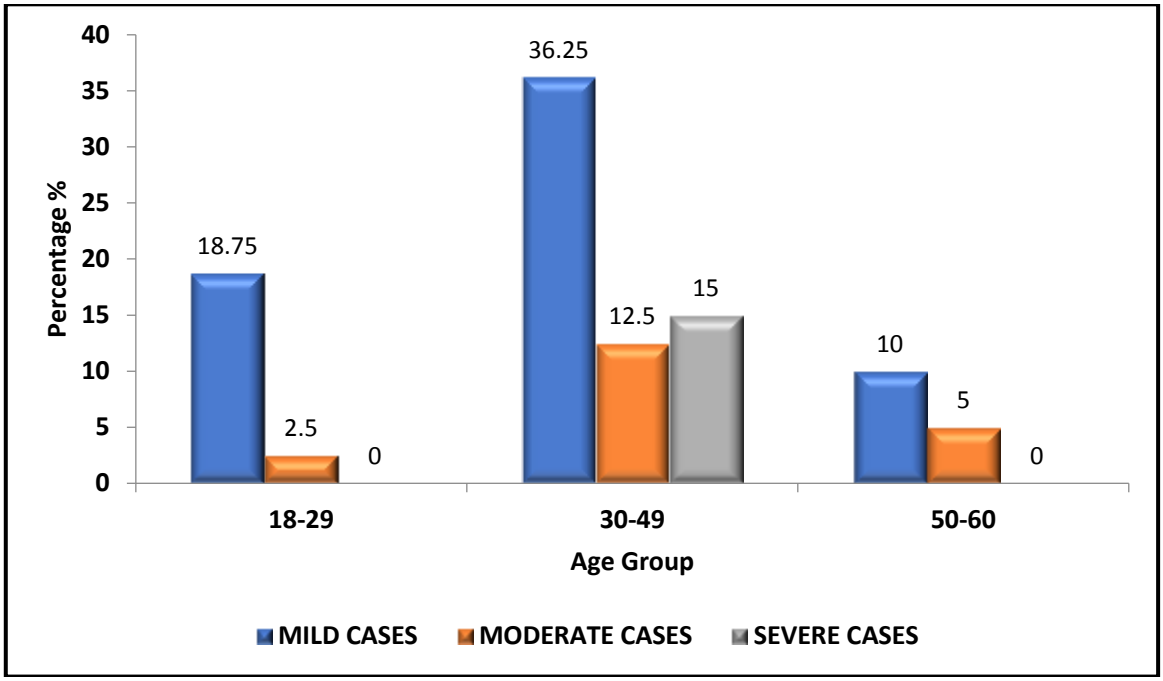


Fig-5: Age Wise Distribution in Relation to PASI.

Among all the 80 patients, the Serum ADA level has a positive corelation with PASI Score in mild cases was 20.74%, in moderate cases it was 28.57% and in severe level it was observed to be 31.70%. as shown in Table 6 and Fig-6.

Table 6: Comparison Of Serum ADAwith Mild, Moderate and Severe Psoriasis in Relation to Pasi Score.

VARIABLES	PASI			p-VALUE
	Mild	Moderate	Severe	
ADA	20.74±2.08	28.57±1.30	31.70±4.10	<0.0001

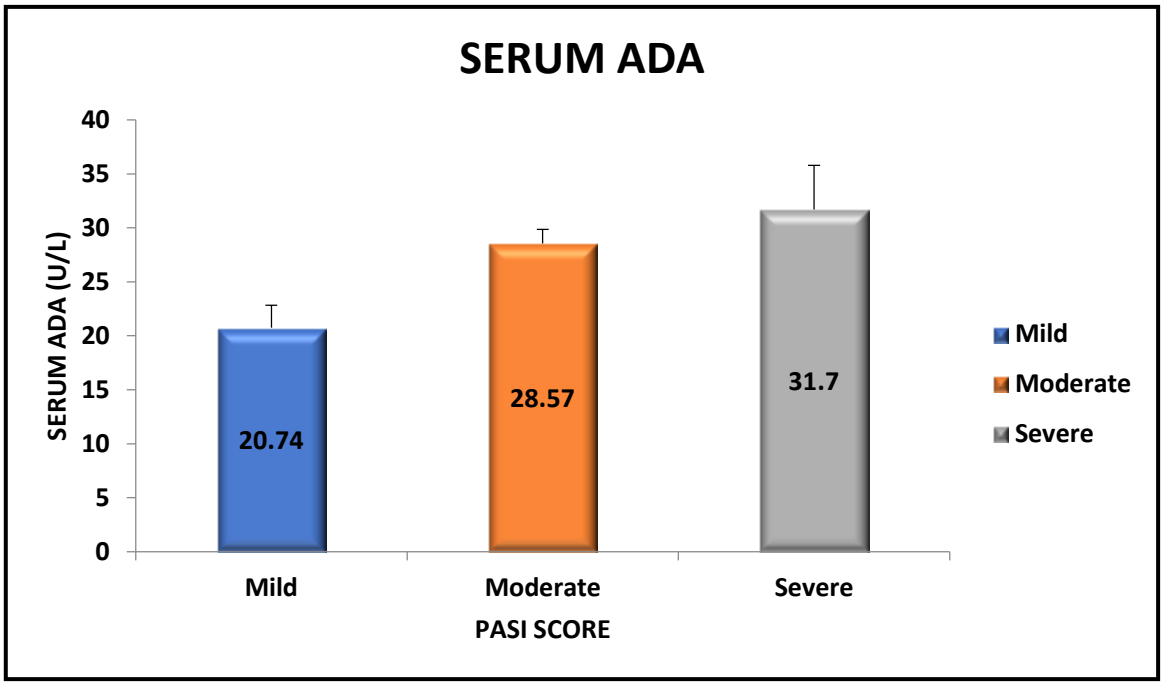


Fig-6: Comparison Of Serum ADAwith Mild, Moderate and Severe Psoriasis in Relation to Pasi Score.

DISCUSSION

Though the etiology of psoriasis still remains unknown, the involvement of immunological disturbances cannot be denied. ADA is widely distributed with the highest activity in T-cells [26]. Studies have shown increased serum ADA levels in diseases characterized by T-cell proliferation or activation [27,28].

Many contradictory results have been reported regarding ADA level in blood lymphocytes, with some studies showing normal and some reporting a higher value. Köse et al noticed decreased ADA activity in plasma and skin tissue from baseline value after treatment of psoriasis for 2 months [29]. Vlcek and Mikulíková reported higher ADA activity in peripheral blood lymphocytes. They also observed a significant decrease in ADA after treatment with methotrexate [30].

In our study, the mean ± SD age was found to be 37.54±10.27 years with the range of 18-60 years. There was another study performed by Kilic et al. [31] reported that mean ± SD age of psoriasis patients was 37.66±14.63, which is nearly consistent with our present study. In a study of Arican O et al. [32] reported mean ± SD age of patients was 35±15.5 which is consistent with our current study. In this study it was found thatthe ratio of males was more as compared to that of the females where out of 80 patients, 24 (30%) patients were female and 56 (70%) patients were male. This study was in accordance to the study performed by the other research investigator Sun Jae Na where the sex ratio of the psoriasis patients was 1.2:1 (male 54.6%, female 45.4%) observing the males ratio to be higher than females [33].

PASI score in the present study was found maximum in mild to moderate cases wherein the age group 30-49, the mild, moderate and severe PASI scorewas36.25%, 12.5% and 15% respectively followed by18-29 years and least in the age group of 50-60 years.It was also noted that the maximum number of psoriasis cases recorded were in the age of 30-49 (51;63.75%) followed by 18-29 (17; 21.25%) and the least was recorded in the age group of 50-60 (12; 15%).

In a study of Kim et al. they studied that 70.45% mild psoriasis and 29.55% had moderate to severe psoriasis patients among 176 psoriasis patients which was to some extent nearly higher than our study. In the present study mean ± SD of serum ADA level was measured in different categories of severity of psoriasis. The mean ± SD level of ADA in psoriasis was 23.95±5.07. The level of ADA in mild psoriasis (PASI≤10) was 20.74±2.08. In moderate (PASI>10-20) the level was 28.57±1.30

and in severe psoriasis (PASI>20)it was 31.70±4.10.(p Value <0.0001), which was in accordance to the study by sultana et al [34]. In accordance to the research work of Murari, Ray & Lodha [35], Khan et al. [36], Nadeem et al. [37] observed that ADA level was elevated in psoriasis patients and its activity was increased according to severity of psoriasis which was statistically significant ($p<0.001$),($p<0.001$), ($p<0.001$) and these findings were consistent with thepresent study. In another study of Hashemi et al. [38] mean ± SD serum ADA level was significantly higher (23±9.06U/L) in psoriasis patients which was nearly consistent to the current study ($p<0.001$).
The elevated plasma ADA activity in psoriasis patients observed in the present study seems to be in accordance with the previously mentioned research whereas Iizuka et al[39]and Koizumi and Ohkawara4 observed a normal ADA level in peripheral blood lymphocytes and serum respectively ($P<0.001$). Erbagci et al reported a drop in ADA after treatment of psoriasis ($P<0.001$).[40] Bukulmez et al found predominantly elevated ADA level in 25 psoriasis patients [41].
In present study we observed a significant association of ADA with severity of disease.
Psoriasis critically influences the psychosocial well-being of patients and reduces their quality of life and work efficiency beyond skin symptoms. However, evidence on the association between life quality based on the Dermatology Life Quality Index (DLQI) and psoriasis severity is limited. Life quality based on DLQI evaluation positively correlated with disease severity among patients with psoriasis, especially among male patients and those with higher body mass index. Therefore, we recommend that clinicians treat the DLQI as an important indicator during patient treatment [42].

Our results may provide insight into the usefulness of ADA as a potential marker of disease severity in psoriasis patients. The finding of the present study suggested that level of serum ADA level in psoriasis patients can be used as a potential marker to predict the severity of the disease.

CONCLUSION

For the purpose of anticipating the severity of psoriasis and monitoring the effectiveness of treatment, serum adenosine deaminase activity can be defined as a potentially useful biomarker. Through the examination of clinical characteristics, PASI determines the severity of psoriasis and varies from clinician to clinician.Additional investigation is required to clarify the fundamental processes that connect ADA dysregulation to the aetiology of psoriasis and to confirm its effectiveness in broader patient populations in various therapeutic contexts. The incorporation of serum ADA testing into standard clinical practice has the potential to improve patient outcomes and standard of quality life and effectiveness of psoriasis care.

ACKNOWLEDGEMENT

I am very much thankful to all my patients for giving me their valuable consent. I am very blessed, grateful and deeply indebted to my honourablePrincipal Dr. Sanjeeb Kakati and the Head of the Department aswell my coguide Dr.Rashmi Rajkakati, my guide Dr. Monigopa Das, Professor of the Department of Biochemistry, Assam Medical College & Hospital Dibrugarh, Assam, India. I am also thankful to my other co guide Dr. Shyamanta Barua, Professor and Head of the Department of Dermatology for his constant guidance. Last but not the least to my Advanced Clinical Biochemistry Laboratory (ACBL Team) for their complete support for sample processing.

Declarations:
Conflicts of interest: There is no any conflict of interest associated with this study
Consent to participate: We have consent to participate.
Consent for publication: We have consent for the publication of this paper.
Authors' contributions: All the authors equally contributed the work

REFERENCES

1. Griffiths CE, Barker J, Bleiker TO, Chalmers R, Creamer D, editors. Rook's textbook of dermatology. 2016; 4 volume set. John Wiley & Sons.
2. Michalek IM, Loring B, John SM .A systematic review of worldwide epidemiology of psoriasis. Journal of the European Academy of Dermatology and Venereology. 2017; 31(2): 205-212.
3. Sunil Dogra, Savita Yadav. Psoriasis in India: Prevalence and pattern. Indian Journal of Dermatology, Venereology, and Leprology. 2010; 76:595-601.
4. Danielsen K, Olsen AO, Wilsgaard T, Furberg AS. Is the prevalence of psoriasis increasing? A 30–year follow-up of a population–based cohort. Br J Dermatol. 2013; 168:1303–10.
5. Bożek A, Reich A. The reliability of three psoriasis assessment tools: psoriasis area and severity index, body surface area and physician global assessment. Adv Clin Exp Med. 2017; 26(5): 851-856.
6. Walsh JA, Arledge T, Nurminen T, Peterson L, Stark J. A Measure of Psoriasis Severity Tested in Patients with Active Psoriatic Arthritis and Treated with Certolizumab Pegol. The Journal of Rheumatology. 2018; 45(7): 922-928.
7. Jain K, Krishna A, Rathore SB .Assessing disease severity by hsCRP as a biochemical marker for psoriasis. International Journal of Research in Dermatology. 2017; 3(4): 501-505.
8. Khan S, Agrawal S, Baral N, Lamsal M. Evaluation of ADA activity as a potential marker of disease severity in psoriasis patients. Psoriasis Targets Ther. 2018; 8:59–63.
9. Adams A, Harkness RA. Adenosine deaminase activity in thymus and other human tissues. Clinical and experimental immunology. 1976; 26(3):647.
10. Zidek Z. Adenosine-cyclic AMP pathways and cytokine expression. European cytokine network. 1999 ;10(3):319-28.
11. Kawada, A.; Tezuka, T.; Nakamizo, Y.; Kimura, H.; Nakagawa, H.; Ohkido, M.; Ozawa, A.; Ohkawara, A.; Kobayashi, H.; Harada, S.; et al. A survey of psoriasis patients in Japan from 1982 to 2001. J. Dermatol. Sci. 2003; 31: 59–64.
12. Takahashi, H.; Nakamura, K.; Kaneko, F.; Nakagawa, H.; Iizuka, H.; Japanese Society for Psoriasis Research. Analysis of psoriasis patients registered with the Japanese Society for Psoriasis Research from 2002–2008. J. Dermatol. 2011; 38:1125–1129
13. Ito, T.; Takahashi, H.; Kawada, A.; Iizuka, H.; Nakagawa, H.; Japanese Society for Psoriasis Research. Epidemiological survey from 2009 to 2012 of psoriatic patients in Japanese Society for Psoriasis Research. J. Dermatol. 2018; 45: 293–301.
14. Naldi, L.; Chatenoud, L.; Linder, D.; Belloni, F.A.; Peserico, A.; Virgili, A.R.; Bruni, P.L.; Ingordo, V.; Scocco, G.L.; Solaroli, C.; et al. Cigarette smoking, body mass index, and stressful life events as risk factors for psoriasis: Results from an Italian case-control study. J. Dermatol. 2005; 125: 61–67.
15. Lindegard, B. Diseases associated with psoriasis in a general population of 159,200 middle-aged, urban, native Swedes. Dermatologica .1986; 172: 298–304.
16. Henseler, T.; Christophers, E. Disease concomitance in psoriasis. J. Am. Acad. Dermatol. 1995; 32: 982–986.
17. Erine A Kupetsky[1], Matthew Keller. Psoriasis vulgaris: an evidence-based guide for primary care. J Am Board Fam Med. 2013 ; 26(6):787-801.
18. Rocha-Pereira, P.; Santos-Silva, A.; Rebelo, I.; Figueiredo, A.; Quintanilha, A.; Teixeira, F. Dislipidemia and oxidative stress in mild and in severe psoriasis as a risk for cardiovascular disease. Clin. Chim. Acta. 2001; 303: N33–39.
19. Uyanik, B.S.; Ari, Z.; Onur, E.; Gunduz, K.; Tanulku, S.; Durkan, K. Serum lipids and apolipoproteins in patients with psoriasis. Clin. Chem. Lab. Med. 2002; 40: 65–68.
20. Pietrzak, A.; Lecewicz-Torun, B. Activity of serum lipase and the diversity of serum lipid profile in psoriasis. Med. Sci. Monit. 2002; 8: CR9–CR13.

21. Salihbegovic, E.M.; Hadzigrahic, N.; Suljagic, E.; Kurtalic, N.; Hadzic, J.; Zejcirovic, A.; Bijedic, M.; Handanagic, A. Psoriasis and dyslipidemia. Mater Sociomed .2015; 27, 15–17.
22. Baker BS, Fry L. The immunology of psoriasis. British Journal of Dermatology. 1992; 126(1):1-9.
23. Louden BA, Pearce DJ, Lang W, Feldman SR .A Simplified Psoriasis Area Severity Index (SPASI) for rating psoriasis severity in clinic patients . J Dermatol. 2004; 10 (2).
24. ADAZYMETM-LS Manufactured by Coral Clinical Systems A Division of Tulip Diagnostics (P) Ltd.
25. Langley RG, Ellis CN .Evaluating psoriasis withPsoriasis Area and Severity Index, PsoriasisGlobal Assessment, and Lattice SystemPhysician's Global Assessment. J Am AcadDermatol.2004; 51:563- 569.
26. Woodley DT, Kim GH. Potential new insight into the pathogenesis of psoriasis. Arch Dermatol. 2009; 145(6):713–714.
27. Koizumi H, Ohkawara A. Adenosine deaminase activity in sera of patients with psoriasis, mycosis fungoides and adult T cell leukemia. Acta Derm Venereol. 1992; 72(6):410–412.
28. Iizuka H, Koizumi H, Kimura T, Miura Y. Adenosine deaminase activity in peripheral lymphocytes of psoriasis and Sézary's syndrome. J Dermatol. 1980; 7(3):165–169.
29. Köse K, Utaş S, Yazici C, Akdaş A, Keleştimur F. Effect of propylthiouracil on adenosine deaminase activity and thyroid function in patients with psoriasis. Br J Dermatol. 2001; 144(6):1121–1126.
30. Vlcek F, Mikulíková D. [The effect of methotrexate on activity of T-lymphocyte marker enzymes in patients with psoriasis vulgaris]. Bratisl Lek Listy. 1995; 96(3):137–140. Slovak.
31. Kılıç S, Reşorlu H, Işik S, Oymak S, Akbal A, et al. Association between mean platelet volume and disease severity in patients with psoriasis and psoriatic arthritis. Advances in Dermatology and Allergology. 2017; 34(2): 126-130.
32. Arican O, Aral M, Sasmaz S, Ciragil P (2005) Serum levels of TNF-α, IFN-γ, IL-6, IL-8, IL-12, IL-17, and IL-18 in patients with active psoriasis and correlation with disease severity. Mediators of Inflammation. 2005; (5): 273-279.
33. Sun Jae Na, Seong Jin Jo, Jai Il Youn. Clinical study on psoriasis patients for past 30 years (1982–2012) in Seoul National University Hospital Psoriasis Clinic. The journal of Dermatology. 2013; 40 (9): 731-735.
34. Suraya S, Debatosh P, Sania H, Mst Shaila Y, Md Saiful I, et al. Role of Adenosine Deaminase in Assessing the Severity of Psoriasis. Ann Rev Resear. 2020; 6(1): 555679.
35. Murari K, Ray A, Lodha R. Adenosine deaminase: A potential biomarker for evaluating the severity of psoriasis. Intenational Journal of Pharma and Bioscience. 2015; 6(4): 629-634.
36. Khan AS, Agrawal S, Baral N, Lamsal M. Evaluation of ADA activity as a potential marker of disease severity in posoriasis patients. Psoriasis: Targets and Therapy. 2018; 8: 59-63.
37. Nadeem M, Mir BA, Shah TA, Waseem M, Dar AH. Hyperuricemia and serum ADA levels in psoriasis and their correlation to severity of disease. International Journal of Contemporary Medical Reaserch. 2019; 6(9): 11-14.
38. Hashemi M, Mehrabifar H, Daliri M, Ghavami S. Adenosine deaminase activity, trypsin inhibitory capacity and total antioxidant capacity in psoriasis. European Academy of Dermatology and Venereolog. 2009; 24(3): 329-334.
39. Iizuka H, Koizumi H, Kimura T, Miura Y. Adenosine deaminase activity in peripheral lymphocytes of psoriasis and Sézary's syndrome. J Dermatol. 1980; 7(3):165–169.
40. Erbagci Z, Erbagci AB, Köylüoglu O, Tuncel AA. Serum adenosine deaminase activity in monitoring disease activity and response to therapy in severe psoriasis. Acta Medica. 2006; 49(2):101.
41. Bukulmez G, Akan T, Ciliv G. Serum adenosine deaminase levels in patients with psoriasis: a prospective case-control study. Eur J Dermatol. 2000; 10(4):274–276.

42. Yiran Chen Lei Wei , Yu Song , Rui Zhang , Le Kuai , Bin Li , Ruiping Wang. Life quality among psoriasis patients based on Dermatology Life Quality Index evaluation and its association with psoriasis severity in China: a cross-sectional study. Ann Med. 2023; 55(1):2231847.