Section: Pulmonary Medicine

Original Research Article

SERUM ADENOSINE DEAMINASE LEVEL IN PATIENTS WITH STABLE AND EXACERBATED CHRONIC OBSTRUCTIVE PULMONARY DISEASE-A COMPARATIVE STUDY.

Ummuhabeeba Kunnoth[1], Rebecca James[2], Ananthothamkandy Amrutha[3]

[1]Assistant Professor, KMCT Medical College, Manassery, India.
[2]Associate Professor, Government Medical College Kozhikode, India.
[3]Assistant Professor, KMCT Medical College, Manassery, India.

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Corresponding Author:
Dr Rebecca James
Email: drrebeccajomy@gmail.com

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality, so it is a major public health concern. There are many modifiable and non-modifiable risk factors for COPD. Identification and correction of modifiable predictors may help in reduction of frequency of exacerbations. Few studies have investigated the factors leading to exacerbations. Decrease of Adenosine deaminase (ADA) activity may play an important role in the formation and treatment of pulmonary injury in COPD patients. Although many reports demonstrated the changes in ADA activity in a whole variety of diseases including tuberculosis, there are few studies in COPD. The purpose of this study was to investigate the effect of serum ADA levels on frequency and severity of exacerbations of COPD. **Objective:** To determine the association of Serum Adenosine deaminase level with acute exacerbation of Chronic obstructive pulmonary disease as compared to stable COPD patients. **Materials & Methods:** This was a cross sectional study which included patients with COPD with age more than 40 years admitted in Pulmonary medicine ward, Intensive care units and patients came for follow up for 12 months (n=114) divided into two groups (n=57).After obtaining informed consent detailed history and pulmonary function test were done Samples for serum adenosine deaminase were collected from study subjects and estimation was done using a photometric method. Statistical analysis was performed using SPSS version 22.0 software. **Results:** Mean Serum adenosine deaminase levels (in U/dL) in Group 1 were significantly low (18.264 +/- 3.353) as compared to Group 2 and the difference was statistically significant.(p value < 0.001).**Conclusion:** Significantly low serum Adenosine deaminase level was seen in acute exacerbation of COPD as compared to stable COPD. This may be a cause of increased level of adenosine that leads to exaggerated pulmonary injury that results in the acute exacerbation of COPD and increased frequency of exacerbation.

INTRODUCTION

Global Burden of Disease Study projected that COPD, which ranked sixth as a cause of death in 1990, became the third leading cause of death worldwide by 2020; a newer projection estimated COPD would be the fourth leading cause of death in 2030. The stable clinical state is by varying degrees of inflammation affecting the large and small airways as well as the alveoli, resulting in mucus hypersecretion, airway narrowing, and alveolar destruction, respectively. With this background of mild inflammation, there is a general belief that exacerbations are episodes where the inflammatory process is enhanced, although the processes involved and their effects are poorly understood.[1]

Adenosine deaminase converts adenosine to inosine. There are two isoenzymes of ADA in serum: ADA1 and ADA2. It has been established that in COPD patients the adenosine levels increase and thus increased pulmonary injury, which can contribute to decrease of ADA activity.[2]

Adenosine deaminase (ADA) catalyses' the conversion of adenosine to inosine in the purine metabolism pathway.[3] Since 1978, when ADA activity was found to be high in tuberculous pleural exudates, ADA has been used in the diagnosis of tuberculosis.[4] The sensitivity and specificity of

ADA were reported 99% and 93% respectively. High ADA levels can also be found in pleural effusions, secondary to other processes or lesions, especially pneumonia, empyema, lymphoma, neoplasia and systemic lupus erythematosus.[5]

MATERIALS AND METHODS

Study Design: Cross sectional study
Duration of study: 12 months (October 1, 2020 to October 1, 2021)
Study setting: Pulmonary Medicine ward, ICU & OPD of Govt. medical college, Kozhikode
Study subjects: Patients admitted with COPD in Pulmonary Medicine ward & ICU and patients came to OPD for follow up at Govt. medical college, Kozhikode
Sample size: Sample size calculation was done using the formula

$$n = \frac{(Z\alpha+Z\beta)^2 SD^2 x2)}{d^2}$$

As the mean values are taken, SD^2 is taken.
So, n=57
Sampling Procedure
Study subjects included patients who are more than 40 years. They were divided into two groups
Group 1:57 patients admitted with acute exacerbation of COPD.
Group 2: 57 patients having stable COPD came for follow up.
Informed consent was taken from all study subjects. Detailed history was taken about the duration of the illness and other significant medical illnesses. Pulmonary function test results were collected from the case records which were done during the admission to assess severity. Samples for serum adenosine deaminase were collected from study subjects and estimation was done using photometric method.
Statistical Analysis
Statistical Package for Social Sciences [SPSS] for Windows, Version 22.0 was used to perform statistical analysis. Mann Whitney Test was used to compare the mean serum ADA levels between the study groups. Furthermore, mean serum ADA levels were compared among the study groups of different categories according to severity was performed using Chi-square test.The level of significance (p-Value)was set at p <0.05.

RESULTS

The mean age of the study patients was with a range of 45–80 years. Most of the Group 1 were distributed in the age group of 45–79 years (mean of 65.04) and Group 2 were between 50-80 years (mean is 63.60). [Table I]
The test results demonstrated that the mean serum ADA level in Group 1 was significantly lesser [22.165 ± 5.72] as compared to Group 2 [28.12 ± 3.166] and the difference was statistically significant at P<0.001*. [Table 2]
Majority of patients were in Gold category A. Among total patients 45.6% of cases were Gold Category A,19.3% were Gold Category B,35.1% Grade C. [Table 3]
The test results showed the mean serum ADA levels in Grade A was 25.42 ± 6.09, Grade B was 21.56 ± 3.25 and Grade C was 18.26 ± 3.353. This difference in the mean serum ADA levels between different gold category grades in case group was statistically significant (p=0.001). [Table 4]
Multiple comparison of mean serum ADA levels between different group showed that Grade A showed significantly higher serum ADA levels as compared to Grade B & C at P=0.04 & P<0.001. However, no significant difference was noted in the serum magnesium levels between Grade B & C [p=0.16]. [Table 5]

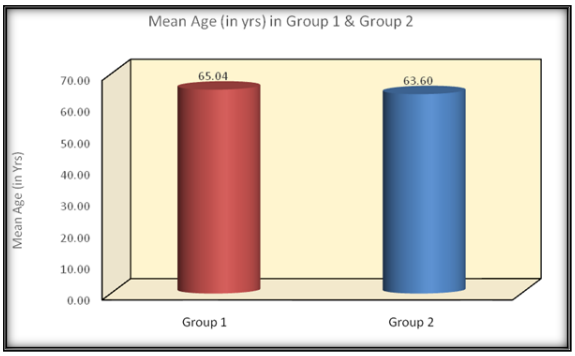

Figure 1: Age distribution in Group1&Group2

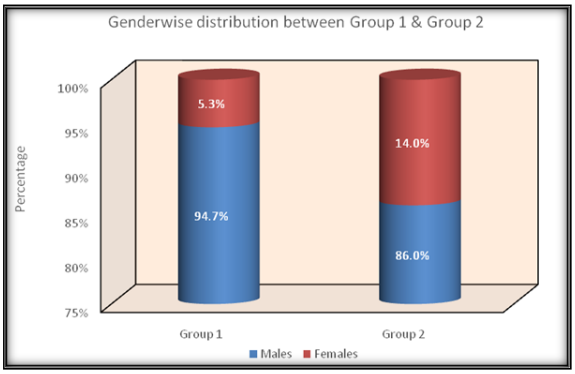

Figure 2: Gender wise distribution between Group1&Group2

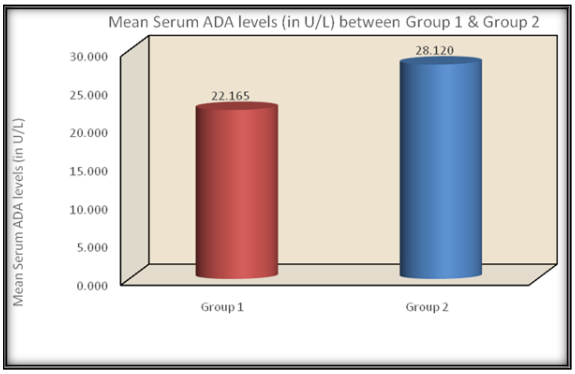

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Figure 3: Comparison of mean serum ADA levels between Group1&Group2

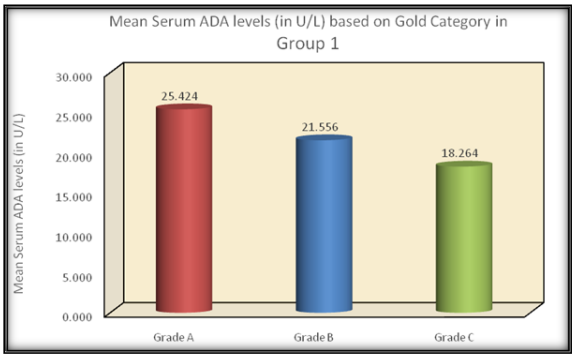

Figure 4:Mean serum ADA levels(U/L) based on Gold Category in Group1

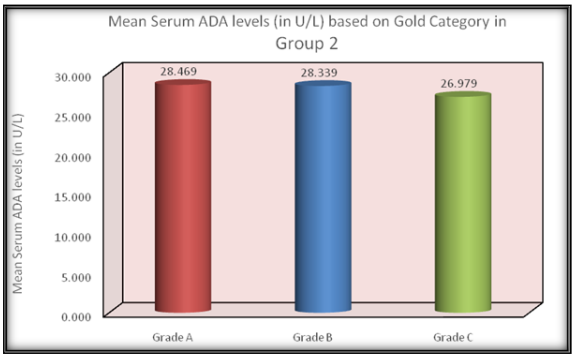

Figure 5: Mean serum ADA levels(in U/L)based on Gold Category in Group2

Table 1: Age and gender distribution among 2 groups

Variable	Category	Group 1		Group 2		P-Value
		Mean	SD	Mean	SD	
Age	Mean & SD	65.04	8.15	63.60	7.87	0.26[a]
	Range	45 - 79		50 - 80		
		n	%	n	%	
Sex	Males	54	94.7%	49	86.0%	0.11[b]
	Females	3	5.3%	8	14.0%	

Table 2: Comparison of mean Serum ADA levels (in U/dL) between Group I and Group 2

Comparison of mean Serum ADA levels (in U/dL) between Group 1 & Group 2 using Mann Whitney Test						
Parameter	**Groups**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Serum ADA	Group 1	57	22.165	5.721	-5.955	<0.001*
	Group 2	57	28.120	3.166		

Table 3: Comparison of Gold Category grading of patients between Group 1 & Group 2 using Chi Square Test

Gold category	Group 1		Group 2		P-Value
	n	%	n	%	
Grade A	26	45.6%	27	47.4%	0.98
Grade B	11	19.3%	11	19.3%	
Grade C	20	35.1%	19	33.3%	

Table 4: Comparison of mean Serum ADA levels based on Gold Category in Group 1

Comparison of mean Serum ADA levels based on Gold Category in Group 1 using Kruskal Wallis Test followed by Mann Whitney's Post hoc Test									
Parameter	**Gold Category**	**N**	**Mean**	**SD**	**Min**	**Max**	**P-Value [a]**	**Sig. Diff**	**P-Value [a]**
Serum ADA	Grade A	26	25.424	6.096	15.63	42.86	<0.001*	A vs B	0.04*
	Grade B	11	21.556	3.247	18.48	28.11		A vs C	<0.001*
	Grade C	20	18.264	3.353	11.30	24.72		B vs C	0.08

Table 5: Comparison of mean Serum ADA levels based on Gold Category in Group 2 using Kruskal Wallis Test

Parameter	Gold Category	N	Mean	SD	Min	Max	P-Value
Serum ADA	Grade A	27	28.469	3.009	22.30	34.90	0.40
	Grade B	11	28.339	3.597	22.65	35.90	
	Grade C	19	26.979	2.096	22.65	29.65	

DISCUSSION

We compared serum ADA level in study groups, and it showed that mean serum ADA level in patients with acute exacerbation of COPD was significantly lesser (22.165 U/L) when compared to stable COPD patients (28.120 U/L) with p value <0.001. Fozard et.al demonstrated elevated level of adenosine in a mouse model of chronic pulmonary inflammation.[6] Elevation in serum adenosine level that was found in this study may reflect low levels of ADA in acute exacerbation of COPD patients.

We also compared serum ADA level in different Gold category patients and it showed that, with the increase in severity, serum ADA level decreased (Mean serum ADA in Gold category A-25.42 U/L,

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category B – 21.56 U/L and category C 18.264) (p value <0.001).The findings of this study suggested that adenosine may contribute to pathogenesis of chronically inflamed asthmatic lungs.[7]We supposed that low activity of ADA in serum of patients with COPD may contribute to high levels of adenosine which may cause change in lung tissue and presumably play an important role in creation of COPD[7] . Hays W. J. Young et al demonstrated that PI purinergic receptor A3R levels are elevated in the lungs of mice that exhibit adenosine-mediated lung disease [7]. Janci et al revealed that controlling adenosine levels with the use of exogenous ADA treatments may provide a significant approach to stop the progression or alter the features of pulmonary fibrosis in Idiopathic pulmonary fibrosis, severe asthma as well as in COPD.[8]

CONCLUSION

- Serum ADA level was found to be significantly lowered in patients with acute exacerbation of chronic obstructive pulmonary disease as compared to stable COPD patients.
- The level of ADA decreased with increasing severity of COPD exacerbation. Multiple comparisons of mean serum ADA levels between different groups showed that the mean serum ADA levels in Gold Category B and C were significantly lesser as compared to category A and the difference was statistically significant. However, no significant difference was noted in the serum ADA levels between Grade B & C.

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Conflict of interest: The authors declare that they have no conflicts of interest.

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