Original Article

Diagnostic Utility of Serum Adenosine Deaminase in Various Pulmonary Diseases

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ABSTRACT

Background: Adenosine deaminase (ADA) is an enzyme that catalyzes the conversion of adenosine to inosine and deoxyadenosine to deoxyinosine. This study was conducted to find the relationship between serum ADA activity and pulmonary diseases such as chronic obstructive pulmonary disease (COPD), bronchial asthma, and pneumonia; and to see whether serum ADA can be used as a diagnostic test for these diseases. **Materials and Methods:** Purposive sampling technique was used and case–control study was conducted among 60 subjects out of which 30 were patients suffering from COPD, bronchial asthma, and pneumonia. Thirty healthy subjects were controls. Analysis was performed using Microsoft Excel 2016 and results were presented in a graphical and tabular form. **Results:** Out of 30 subjects, 50% (n = 15) patients suffered from COPD, 33.33% (n = 10) patients suffered from bronchial asthma, and 16.67% (n = 5) suffered from pneumonia. The serum ADA activity for COPD, bronchial asthma and pneumonia were 19.31 ± 1.67, 16.68 ± 1.75, and 18.11 ± 2.19, respectively. ADA activity in serum of patients was found to be significantly decreased as compared to the healthy controls ($P \leq 0.05$). **Conclusion:** The present study suggests that ADA activity tends to decrease in COPD, bronchial asthma, and pneumonia. Decrease in ADA causes accumulation of adenosine and its subsequent effects such as bronchoconstriction. The balance between ADA and the levels of adenosine in serum may result in pathogenesis of these diseases. The measurement of serum ADA, which is relatively easy, at the time of hospital admission, may provide additional diagnostic information on the etiology and treatment of these diseases.

Key words: Adenosine deaminase, asthma, chronic obstructive pulmonary disease, pneumonia

INTRODUCTION

Adenosine deaminase (ADA) is an enzyme that catalyzes the conversion of deoxyadenosine to deoxyinosine and adenosine to inosine. ADA is required to differentiate lymphoid cells, especially T lymphocytes and plays a role in the conversion of monocytes into macrophages.[1] The important purpose of this enzyme is in immune system cells, the ADA activity in T lymphocytes is 5-20 fold more than B lymphocytes.[2] Measurement of the activity of ADA in body fluids is a useful diagnostic method. The activity of ADA is proportionate to T lymphocyte activity.[2] Extracellular adenosine is a signaling molecule, produced as a consequence of cell damage and further regulates tissue injury and repair. According to this, adenosine levels are elevated in the lungs of patients with chronic obstructive pulmonary disease (COPD), where it is hypothesized to manage the balance between tissue repair and excessive airway remodeling.[3] It has been proven that in COPD patients the adenosine levels increase, which may lead to decrease of ADA activity.[4]

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As stated by the World Health Organization (WHO), 65 million people suffer from moderate to severe COPD and deaths due to COPD in 2005 was over 3 million, which represents 5% of all deaths worldwide. Almost all of the knowledge on COPD prevalence comes from developed countries however, even in developed countries; accurate data on COPD epidemiology are difficult and costly to collect. It is a fact that just about 90% of COPD deaths occur in countries with lesser incomes. Previously, mostly men were affected by COPD, but lately, due to higher tobacco consumption by women in financially richer countries and increased use of fuel/gas for cooking contributing to indoor air pollution in financially poorer countries, COPD currently affects men and women equally.[5] In 2002, COPD was the 5th most common cause of mortality. COPD mortality is expected to rise by over 30% in 10 years unless immediate action is taken to cut back the risk factors, the most important being tobacco use. Show that by 2030, COPD will be the 3rd leading cause of death globally, will be COPD by 2030 as shown by various estimates.[5] Till 2016, 3 out of five leading causes of deaths were caused by non-communicable diseases and now, COPD is the 2nd largest cause of death in India. The prevalence ranged between 2% and 22% among the men and 1.2–19% among women in several different population-based studies all over India.[6]

Asthma is a chronic lung disease characterized by repeated attacks of dyspnea along with wheezing, which differs in severity and frequency among different patients. These attacks may occur many times in a day, and for some patients becomes worse during exercise or at night time.[7] As stated by the WHO, approximately 235 million people across the world are asthmatics. Asthma is a public health problem of both the developed countries such as the USA and UK and developing countries such as India and Bangladesh. Over 80% of mortality due to asthma occurs in developing and lesser income countries. Asthma is often diagnosed late and inadequately treated, creating a considerable burden to patients and their families and thereby decreasing the patient's potential to work for a lifetime.[7]

Pneumonia is the inflammation of lungs caused by bacterial or viral infections. The common mode of transmission is by direct contact with the patient or infected person.[8] In pneumonia, pus and other fluids collect in the alveoli, which cause dyspnea and limits oxygen intake. Pneumonia affects children and families all over the world, but is prevalence is higher in South Asia and sub-Saharan Africa.[8]

This study aimed to find out the relationship between serum ADA and the above-mentioned disorders and to work out whether serum ADA can be used as a screening test to assist in the diagnosis and the contribution of this enzyme in various pulmonary diseases.

Aim

With this background, this study aimed to study the diagnostic utility of Serum ADA in various pulmonary diseases such as COPD, bronchial asthma, and pneumonia.

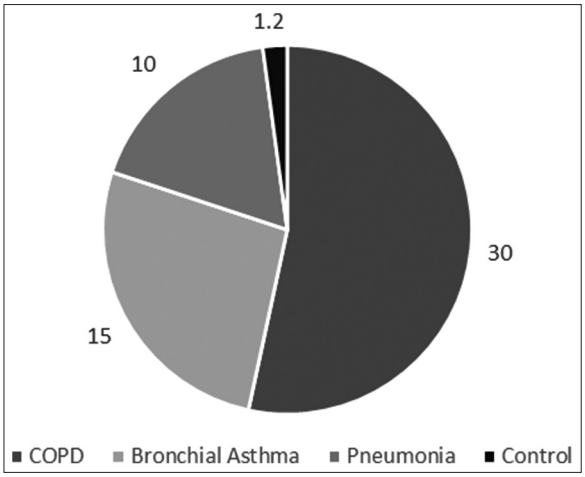
Objectives

The objectives are as follows:

a. To estimate Serum ADA levels in subjects with COPD, bronchial asthma and pneumonia and compare them with age- and sex-matched controls
b. To observe the association of Serum ADA with various pulmonary diseases.

MATERIALS AND METHODS

This study was a retrospective study that was performed between April 2019 and June 2019. The type of study was case–control study. The sampling type was purposive. The age of the participants was between 18 and 70 years. A total number of 60 subjects were studied out of which 30 were cases of pulmonary diseases who had fulfilled the inclusion and exclusion criteria. Remaining 30 subjects were healthy, age- and sex-matched controls. Data were collected using a prepared pro forma sheet which included name, age, vitals, serum ADA level, and any other additional pulmonary findings. This study was carried out in the department of biochemistry**.** The volunteering subjects were required to fill up a "Informed Consent Form" which was duly signed by the volunteer himself/herself, two witnesses, and the principle investigator. Details regarding age, sex, and clinical presentation were collected. 2 ml of venous blood was collected in Plain Vacutainer from all 60 subjects for ADA estimation. Serum ADA estimation was done by Colorimetric method. The blood collection and assessment were performed at Central Clinical Laboratory. This study was approved by the Institutional Ethics Committee. Data obtained were then analyzed to establish a relationship between serum ADA level and various pulmonary diseases. Statistical analysis was done with appropriate tests like unpaired t-tests in consultation with a statistician using Excel 2016 software. Results were presented in a graphical and tabular form. The significance was set at $P < 0.05$.



Graph 1: Number of subjects

RESULTS

The mean age of the all 30 patients was 46 years with a standard deviation of 17.97 years. The age of COPD, bronchial asthma, and pneumonia patients differed significantly. There was no significant correlation between age, sex, and serum ADA levels. Out of 30 subjects, 50% (n = 15) patients suffered from COPD, 33.33% (n = 10) patients suffered from bronchial asthma and 16.67% (n = 5) suffered from pneumonia as shown in Graph 1. The mean age of COPD patients was 58.93 ± 8.66 years, bronchial asthma patients was 39.6 ± 15.01 years, and pneumonia patients was 20 ± 1.41 years.

The mean serum ADA levels of patients and controls are given in Table 1. The serum ADA levels were lower in the patients with pulmonary diseases. The serum ADA levels were higher in the case of all the individuals in the control group.

Serum ADA activity in patients of all three diseases was lower than those in normal individuals significantly (P < 0.05), as shown in Table 2.

However, these levels did not significantly differ between COPD patients and pneumonia patients (P = 0.36); and between bronchial asthma and pneumonia patients (P = 0.29).

A significant difference in serum ADA activity was found between COPD and bronchial asthma (P < 0.05) as shown in Table 3. The serum ADA levels were higher in patients of COPD than in patients of bronchial asthma.

Table 1: Serum ADA activity of patients and controls

Study subjects	COPD	Bronchial asthma	Pneumonia	Control
Mean ADA level	19.31	16.68	18.12	22.03
Standard Deviation	1.67	1.75	2.19	2.81

COPD: Chronic obstructive pulmonary disease, ADA: Adenosine deaminase

Table 2: Comparison between controls and pulmonary diseases

t-test: Two-sample assuming unequal variances	*P*-value
Control and COPD	0000003.796
Control and bronchial asthma	0000004.552
Control and pneumonia	0.017880623

COPD: Chronic obstructive pulmonary disease

Table 3: Comparison between COPD and bronchial asthma

t-test: Two-sample assuming unequal variances	COPD	Bronchial asthma
Mean	19.30933333	16.68
Variance	2.992492381	3.403311111
Observations	15	10
Hypothesized mean difference	0	
df	19	
t-Stat	3.57863081	
P (*t*≤*t*) one-tail	0.001001751	
t Critical one-tail	1.729132812	
P (*t*≤*t*) two-tail	0.002003502	
t Critical two-tail	2.093024054	

COPD: Chronic obstructive pulmonary disease

DISCUSSION

In our study, ADA activity in serum of patients was found to be significantly decreased as compared to the healthy controls (P ≤ 0.05). In a study conducted by Goodarzi *et al*., they found low activity of ADA in COPD patients which is similar to the results obtained in this study. Adenosine and its receptor levels are increased in the lungs of patients with COPD and asthma.[4] Hence, low ADA levels may contribute to the elevated levels of adenosine in these patients. Adenosine is an omnipresent, powerful signaling molecule, which accumulates at the time of cellular damage. When inflammation occurs, the catabolic breakdown of ATP leads to the formation of adenosine. It regulates the inflammatory reaction with the help of adenosine receptors.[4] Decrease of ADA activity may have a critical role in formulating newer treatment options for COPD patients. According to study conducted by Jindal, COPD being a chronic, progressive disease results in a substantial financial burden on hospitals and the individual. At individual level, it is almost always not feasible to treat for patients from a lower socio-economic class. Due to poor availability of spirometry, secondary, and tertiary prevention of COPD is difficult. Chest radiography which is commonly used for follow-up of COPD by practitioners does not represent the stage of the disease to its fullest

extent. The precise findings of hyperinflation and early emphysema are repeatedly missed on plain chest radiographs.[9] Thus, a simple test of ADA estimation may provide additional information to help in the diagnosis of COPD. This study also found significantly low values of serum ADA in patients of pneumonia as compared. This is in contrast to a study conducted by Nayak *et al*., where serum ADA activity was found to be higher.[10] This study also found low values of serum ADA activity in patients of bronchial asthma and these values were similar to a study conducted by Markova and Markova; however, the values were higher as compared to controls in their study.[1] In another study conducted by Poddar and Sharma *et al*., the serum ADA activity was significantly decreased as compared to controls.[11,12] Thus, the activity of serum ADA was found to be variable in patients of bronchial asthma in various studies. The pathophysiological mechanism for this increase in activity is still unclear; however, the decrease in serum ADA activity can be attributed to the accumulation of adenosine in the patients of bronchial asthma which caused symptoms like shortness of breath due to bronchoconstriction. This concept can be used in making newer drugs that can enhance the activity of serum ADA in asthmatics. A new finding of significant difference in the values of serum ADA in COPD and bronchial asthma was also noted in this study.

CONCLUSION

The present study suggests that ADA levels tend to decrease in COPD, bronchial asthma, and pneumonia. Decrease in ADA leads to accumulation of adenosine and its subsequent deleterious effects such as bronchoconstriction. The balance between ADA and the levels of adenosine in serum may result in pathogenesis of these diseases. Moreover, this study was conducted on a small sample size so ADA can be studied more if a bigger sample size is considered. Serum ADA was found to be a marker for differentiating between COPD and bronchial asthma for which further studies must be conducted. The measurement of serum ADA, which is relatively easy and sensitive, at the time of hospital admission, may provide additional diagnostic information on the etiology and treatment of COPD, bronchial asthma, and pneumonia.

REFERENCES

1. Markova R, Markova AP. Diagnostic value of serum adenosine deaminase. Int J Pharm Sci Invent 2017;6:6-7.
2. Boloursaz M, Khalilzadeh S, Khodayari A, Hakimi S. Adenosine deaminase level as an indicator for differentiating between active pulmonary tuberculosis infection and other pulmonary infections. J Compr Pediatr 2012;3:3-6.
3. Zhou Y, Murthy JN, Zeng D, Belardinelli L, Blackburn MR. Alterations in adenosine metabolism and signaling in patients with chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis. PLoS One 2010;5:e9224.
4. Goodarzi MT, Abdi M, Tavilani H, Nadi E, Rashidi M. Adenosine deaminase activity in COPD patients and healthy subjects. Iran J Allergy, Asthma Immunol 2010;9:7-12.
5. Chronic Respiratory Diseases. Available from: http://www.who.int/respiratory/copd/en. [Last accessed on 2021 Jun 04].
6. Hossain MM. Burden of chronic obstructive pulmonary disease in India: Status, practices and prevention. Int J Pulm Respir Sci 2018;2:1-4.
7. Chronic Respiratory Diseases: Asthma. Available from: https://www.who.int/respiratory/asthma/en. [Last accessed on 2021 Jun 04].
8. Pneumonia. Available from: https://www.who.int/topics/pneumococcal_infections/en. [Last accessed on 2021 Jun 04].
9. Jindal SK. COPD: The unrecognized epidemic in India. J Assoc Physicians India 2012;60:14-6.
10. Nayak BS, Mohammed N, Ramnanansingh TG, Nayak AS. Determination of adenosine deaminase levels in patients with and without community acquired pneumonia a Trinidadian study. Endocrinol Diabetes Res 2018;4:2.
11. Sharma J, Menon BK, Vijayan VK, Bansal SK. Changes in adenosine metabolism in asthma. A study on adenosine, 5 & #39-NT, adenosine deaminase and its isoenzyme levels in serum, lymphocytes and erythrocytes. Open J Respir Dis 2015;5:33-49.
12. Poddar A. Serum adenosine deaminase activity: A possible explanation for hyperactive immune status and onset of nephropathy in diabetic subjects. Int J Pharm Res Bio Sci 2015;4:328-35.

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