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ORIGINAL ARTICLE

Estimation of Serum Adenosine Deaminase-2 (ADA2) as One of the Non-Invasive Diagnostic Marker of Pleural Effusion in Systemic Lupus Erythromatosus

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ABSTRACT

Background: Systemic Lupus Erythromatosus (SLE) is an autoimmune disorder which disturbs the normal life of human due to involvement of different vital organs like bones, lungs, heart & kidney etc. A pleural effusion is one of the most common complications associated with lung involvement in young female patients with SLE. Pleural fluid examination is the main method for diagnosis, but lack of trained people and limited resources necessitate evaluating the non-invasive cheap method.

Objective: To estimate the serum ADA2 level as one of non invasive marker for the diagnostic tool of pleural effusion in SLE

Methodology: There were 29 female cases of SLE diagnosed in different remote areas of Pakistan divided into two groups: group-I contained 16 diagnosed cases of SLE without pulmonary involvement, and group-II contained 13 diagnosed cases of SLE with pleural effusion. The serum ADA2 level was estimated by using the ELISA method by using sandwich technology in conjunction with the ELISA method. In order to conduct the statistical analysis of the data, SPSS version 22 was used to apply an independent Student t-test.

Results: The mean serum ADA2 of group-I was 15.1 ± 2.14 U/L while mean value of serum ADA2 of group-II was 11.13 ± 1.76 U/L. There was statistical ($p<0.05$) decreased level of serum ADA2 in patients of group-II patients with compared the patients of group-I patients.

Conclusion: Serum ADA2 level in the serum may be one of diagnostic marker for the diagnosis of pleural effusion in the patients of SLE

Keywords: SLE , Pleural Effusion, ADA Enzyme, ADA2,

INTRODUCTION

Involvement of vital organs of the human body is one of the main causes of Systemic Lupus Erythromatosus (SLE). Many parts of the world now report SLE affecting the lungs in young people between 30 and 40 years of age.[1,2] A common respiratory complaint associated with SLE is pleuritis.[3] Approximately 40 -60% of patients with SLE suffer from pleurisy of the lungs.[4]

In the early stages of SLE, the clinical manifestations are sometimes silent; the patient has no complaints. But lung involvement as a complication has begun and ultimately led to pleural effusion. [6] As a result of a radiological examination, the pleural effusion caused by SLE may appear to be a pleural effusion related to congestive cardiac failure, airway cancer, lung infection or tuberculosis lung pleural effusions. [7,8]

The main challenge is to diagnose lung pleural effusion due to SLE so that proper treatment can be provided. As a result of the examination of pleural fluid, there are high neutrophil and lymphocyte concentrations and decreases of C3 & C4 levels, which are helpful tools for the diagnosis of pleural effusion caused by SLE.[9] However, taking pleural fluid samples is a very painful and competitive procedure. Currently, researchers are seeking the best non-invasive technique to diagnose pleural effusion caused by SLE.

The enzyme adenosine deaminase (ADA) is one of the most important enzymes in purine metabolism.[10] It is easy to find this enzyme in bacteria, vertebrates, plants, and mammals due to its high conservation of amino acids. [11] Human immune system is maintained by ADA.[12] ADA has two isoforms, ADA1 and ADA2; ADA1 is found in lymphocytic fluids, while ADA2 is found in plasma and serum.[13] Arthritis and psoriasis cause elevated ADA levels in blood plasma, whereas lung fibrosis causes decreased levels. [14, 15]

The aim of this study was to evaluate and compare the levels of the ADA2 in blood plasma of SLE patients with and without pleural effusion in this study.

METHODOLOGY

The case comparative study was conducted at the Fatima Jinnah Institute of Chest Diseases in Quetta between January 2021 and June 2021. There were 29 cases of SLE enrolled in this study according to inclusion and exclusion criteria with their own consent, and they were divided into two groups, group-I contains 16 cases of SLE without pulmonary complications, while group-II contains 13 cases of SLE with plural effusionsSLE cases were diagnosed by consultant rheumatologists, while pleural effusion cases were diagnosed by consultants pulmonologists based on clinical and radiological examinations. Among the cases of SLE in Pakistan, Sindh, Punjab, and Balochistan were selected. In the present study, all female patients aged 30 to 50 years with no articular manifestations of SLE with a history of SLE at least for the last three years and with ANA profile positivity were included in the study, whereas patients with SLE aged less than 20 years or more than 50 years, with joint involvement, hepatic malformations, any history of renal disorders, and males with SLE were excluded from the study.

Adenosine Deaminase-2 (ADA2) is estimated from 3cc of blood drawn from the cuboidal vein under septic conditions. Chromatography, ELSIA, Enzymatic essay, and Caloric method can be used to estimate serum ADA2. A sandwich method was used in our study in order to estimate ADA2 by the ELISA method.[16] There is a cut off value of 14.0 U/L for serum ADA2 levels. As part of the statistical analysis of the data, SPSS version 22 was used to apply an independent student t test to the data.

RESULTS

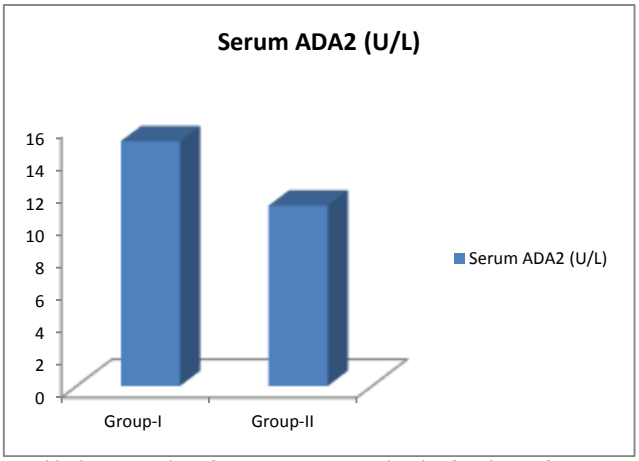
Total 29 female cases of SLE were selected from different cities of Pakistan, these patients were divided in to two groups. Group-I had 16 diagnosed cases of SLE without pulmonary manifestation while group-II had 13 cases of SLE with pleural effusion. The mean serum ADA2 of group-I was 15.1 ± 2.14 U/L while mean value of serum ADA2 of group-II was 11.13 ± 1.76 U/L.

There was statistical ($p<0.05$) decreased level of serum ADA2 in patients of group-II patients with compared the patients of group-I patients.

Table 1: Parameters for SLE patients of Group-I & Group-II Patients

Parameter	Group-I	Group-II
ANA Profile	Positive (++)	Positive (+++)
ESR	110 ± 8.0	112 ± 7.0
RA factor	Negative	Negative
Serum ADA2 (U/L)	15.1 ± 2.14	11.13 ± 1.76 *

(* $p<0.05$)



Graphical Presentation of Mean Serum ADA2 levels of Patients of Group-I & Group-II

DISCUSSION

Even up to several years into the course of the disease, most patients with pulmonary manifestations of SLE are asymptomatic. However, 7.5-11% of patients with pulmonary manifestations of SLE develop symptoms.[17] The lungs are commonly involved as a complication of the autoimmune diseases such as SLE. There are several complicated manifestations of SLE, but the most common one is pleural effusion.[18] Various etiologies of pleural effusion exist in this age group, so different markers are needed to differentiate SLE-related pleural effusion from other clinical pathologies.

Lymphocytes are responsible for producing the enzyme ADA, which takes part in the purine metabolism.[10] This enzyme acts as a catabolic agent in the purine catabolism from adenosine to inosine in the body.[19] Adenosine deamination by ADA suppresses inflammation by deaminating adenosine.[20] Thus, ADA acts as an anti-inflammatory agent. It also regulates the maturation of immune cells like lymphocytes and cell differentiation. [21,22]

It is noted that the levels of ADA enzyme are high in pleural fluid samples of patients who have pleural effusions caused by pulmonary tuberculosis, SLE, lung cancer, etc. along with an elevation of lymphocytes and a suppression of C3 and C4.[9] For proper diagnosis, the serum level of ADA enzyme is variable, for instance, its level increases in lung fibrosis caused by tuberculosis, its level also increases in general SLE patients, and some studies have shown decreased levels of ADA in SLE patients.

ADA1 and ADA2 are the two isoforms of the ADA enzyme. In lymphocytes, ADA1 is present, while in blood plasma and serum, ADA2 is present. There have been studies done on estimating the level of ADA enzyme in pulmonary tuberculosis, lung fibrosis, and SLE patients from the sample of pleural effusion, but very few are available for serum measurementThe ADA1 isoform exists in pleural effusions, while the ADA2 isoform exists in serum. [11,12]

In their study, Chen DY et al. (2021)[9] found that pleural effusion with SLE is easily recognized by decreased levels of C3 & C4 (and high lymphocyte levels) and increased levels of ADA (in the pleural fluid sample). It is not possible for our research areas to aspirate pleural effusion from every suspected patient with SLE or from every patient with SLE suffering from SLE. Because most patients with SLE, even those diagnosed, remain asymptomatic at the time of their presentation, some serum or blood plasma parameter is required to give a clue regarding the development of complications. This study may be useful in the future in this regard, since it showed a significant decline in serum ADA2 levels in patients with pleural effusion and SLE.

As well, Porcel JM et al. (2021)[23] noted that level of ADA level in pleural fluid increased in patients with pleural effusion, but no confirmation of pleural effusion was seen on ANA profile, which is a costly test. We do not have access to ANA profiles on the spot in our remote areas, so evaluating serum ADA2 gives strong suspicion regarding the development of pleural effusions in SLE patients.

Some limitations of our study include a small sample size, few cases from different regions of Pakistan, and a lack of genetic analysis. A proper center of autoimmune diseases at central cities of Pakistan will need to study different isoforms of ADA enzyme on a large sample size in the future. In addition, genetic correlations between SLE patients need to be analyzed.

CONCLUSION

It is thought that the serum level of ADA2 in serum may be useful as a diagnostic marker for the diagnosis of pleural effusions in patients with SLE.

Conflict of Interest: There is no any conflict of interest.

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