ISSN 2394–806X
IJHRMLP, Vol: 01 No: 02 June, 2015
Printed in India




ORIGINAL PAPER

# Study on Changes in Serum Adenosine Deaminase Activity in Patients with Hepatitis

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***Received** on March 23/2015; **accepted** (revised) on March 30/2015; **approved** by author on May 11/2015*

## ABSTRACT

*A case control study was undertaken to find out the significance of serum adenosine deaminase activity in hepatitis, to correlate the changes in serum adenosine deaminase activity with respect to other liver function tests and to evaluate its clinical usefulness in diagnosis of hepatitis. Out of total 60 subjects, 30 healthy individuals were taken as control group and 30 cases of different types of hepatitis were taken as test group. The serum Adenosine deaminase and liver function tests were done by colorimetric methods. The mean serum adenosine deaminase activity in control group and the test group were found to be 21.3+3.69 U/L and 73.3+18.33 U/L respectively with a significance of P<0.001. Positive correlation have been found between adenosine deaminase and some parameters of liver function tests such as total bilirubin and serum transaminases in hepatitis which is significant with P<0.05. So, serum adenosine deaminase activity in hepatitis is significantly raised than that in the normal healthy persons and is increased with increasing levels of serum transaminases and total bilirubin levels. The study concluded that determination of serum adenosine deaminase along with liver function test would increase both the sensitivity and the specificity of laboratory tests in the detection of hepatitis.*

***Keywords:** Case Control Study, Adenosine Deaminase, Hepatitis, Liver Function Test*

## INTRODUCTION

Hepatitis can be described as an inflammatory process in the liver characterized by diffuse or patchy hepatocellular necrosis affecting all acini. Acute hepatitis is when it lasts less then 6 months and chronic hepatitis is when it persists longer. A group of virus, known as hepatitis virus (A, B, C, D and E) cause most cases of liver damage worldwide. Hepatitis can also be due to toxins (notably alcohol) or from autoimmune process, hepatitis due to metabolic diseases (Wilson's disease), ischemic hepatitis, non-alcoholic steatohepatitis, hereditary ($á_1$-antitrypsin deficiency, hereditary hemochromatosis), etc. Epidemics of liver disease were recorded, as long ago as Hippocrates' time and, despite major advances in diagnosis and prevention methods over the past two decades, viral hepatitis remains one of the most serious global health problems facing humans today.

Liver tests rarely suggest a specific diagnosis; rather, they suggest a general category of liver disease, such as hepatocellular or cholestatic, which then further directs the evaluation. The liver carries out thousands of

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biochemical functions, most of which cannot be easily measured by blood tests. Laboratory tests measure only a limited number of these functions. In fact, many tests, such as the aminotransferases or alkaline phosphatase, do not measure liver function at all. Rather, they detect liver cell damage or interference with bile flow. Thus, no test enables the clinician to accurately assess the liver's total functional capacity. To increase both the sensitivity and the specificity of laboratory tests in the detection of liver disease, it is best to use them as a battery. Due to the above shortcomings, there is a continuous search for a test along with the existing liver function tests, which also gives a picture of the pathogenesis of the liver disease. Testing for serum adenosine deaminase level in hepatitis gives us an idea about the mononuclear cell infiltration and lymphocytic proliferation that occurs in hepatitis along with hepatocyte damage.

Adenosine deaminase is an enzyme involved in the catabolism of purine bases, capable of catalyzing the deamination of adenosine, forming inosine in the process.[1] Its main physiologic activity is related to lymphocytic proliferation and cell mediated immune response.[2,3] It was reported that high serum adenosine deaminase activities were observed in patients with acute hepatitis, alcoholic hepatic fibrosis, chronic active hepatitis, liver cirrhosis and hepatoma.[4] The elevated serum adenosine deaminase activity in patients with hepatitis may reflect the phagocytic activity of macrophages and proliferation of lymphocytes, and may provide useful additional diagnostic information on the pathogenesis of hepatitis. In view of the above, the present study is undertaken to evaluate the value of adenosine deaminase activity in various types of hepatitis and correlate the values with other liver function tests.

## MATERIALS AND METHODS

The present study was designed as a case control, hospital based study in a tertiary care medical college and hospital. Two groups of subjects selected for the study are as follows:

**1. Control group:** In the control group, only those subjects were selected who gave no history suggestive of hepatitis or any major illness in the recent past and in whom clinical examination did not reveal any abnormality relating to any system. There were 22 male and 8 female subjects with age ranging from 10 years to 60 years. Among the subjects selected, healthy individuals, age and gender matched for the patients, were included as controls. All individuals of the control group co-operated voluntarily.

**2. Experimental or Test group:** In these groups' 30 cases of different types of hepatitis including viral, toxic, alcoholic and autoimmune hepatitis was taken with prior informed consent. There are 23 males and 7 females in the experimental group. The cases were selected on the basis of the following criteria:

(a) History and findings suggestive of hepatitis namely fever, malaise, anorexia, nausea, vomiting, pain in the right upper abdomen, high colored urine, jaundice, tender hepatomegaly, etc.

(b) Biochemical evidence of damaged liver function with serum total bilirubin level more than 1.2 mg/dl.

(c) It was also ensured that the patients did not have other diseases such as diabetes mellitus, cardiovascular diseases, hypertension, kidney disease, etc.

**The following investigations were done in each of the cases**:

1) Serum adenosine deaminase estimated by MICROXPRESS ADA- MTB kit dependent on Giusti method.[5]

2) **Liver function profile**:
   i) Total serum bilirubin estimated by Modified Jendrassik and Grof's method.[6]
   ii) Total protein measured by Biuret method.[7, 8]
   iii) Albumin estimated by Bromocresol green method.[9]
   iv) Serum alanine aminotransferase (ALT or SGPT) estimated by Modified International Federation of Clinical Chemistry (IFCC) method.[10]
   v) Serum aspartate aminotransferase (AST or SGOT) determined by IFCC method.[10, 11]

## RESULTS AND OBSERVATION

**Age and sex distribution of subjects**: In the control group, the age of the subjects ranged from 10 to 60 years, with a mean of 34.6 years and a standard deviation of 11.69. The majority of them belonged to third decade constituting 33.3% of the total. Out of a total of 30 controls 22 were male (73.4%) and 8 were female (26.6%). The age

of the patients ranged from 10 years to 60 years, with a mean of 34.7 years and a standard deviation of 10.9. The peak incidence of the disease was observed in the age group of 20 to 29 years (36.7%) followed by 30 to 39 years (26.7%) and 40 to 49 years (23.3%). Out of a total of 30 cases 23 were male (76.7%) and 7 were female (23.3%).

**Table 1** Age and sex wise distribution of subjects

| Variables | | Group | | | |
|---|---|---|---|---|---|
| | | Control | | Test | |
| | | Number of cases | Percentage | Number of cases | Percentage |
| Age in years | 10–19 | 2 | 6.7 | 1 | 3.3 |
| | 20–29 | 10 | 33.3 | 11 | 36.7 |
| | 30–39 | 8 | 26.7 | 8 | 26.7 |
| | 40–49 | 6 | 20 | 7 | 23.3 |
| | 50–60 | 4 | 13.3 | 3 | 10 |
| Sex | Male | 22 | 73.4 | 23 | 76.7 |
| | Female | 8 | 26.6 | 7 | 23.3 |

**Etiology of hepatitis:** Maximum of the hepatitis cases are of viral origin with a percentage of 63.3%. Majority of the viral hepatitis cases have hepatitis A with a percentage of 47.4 %.

**Serum adenosine deaminase activity in hepatitis**: **Figure 1** shows that majority of the patients with hepatitis were having ADA more than 80 U/L. Very few cases were having ADA below 60 U/L. Moderate number of cases were having ADA in between 60 to 80 U/L.

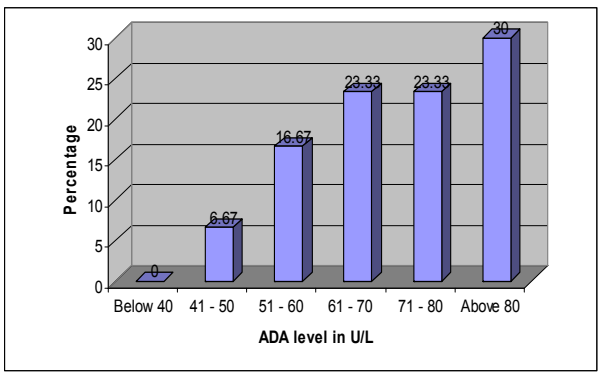


**Figure 1** Percentage distribution of ADA in hepatitis

**Table 2** Results of estimated serum adenosine deaminase under different conditions in control and experimental groups with their mean values and statistical parameters

| Control group (A) | | | | Experimental group | | | |
|---|---|---|---|---|---|---|---|
| Serial No. | ADA (U/L) | Serial No | ADA (U/L) | Serial No | ADA (U/L) | Serial No | ADA (U/L) |
| 1 | 22 | 16 | 23 | 1 | 46 | 16 | 85 |
| 2 | 15 | 17 | 25 | 2 | 56 | 17 | 72 |
| 3 | 21 | 18 | 24 | 3 | 121 | 18 | 64 |
| 4 | 25 | 19 | 25 | 4 | 61 | 19 | 101 |
| 5 | 22 | 20 | 22 | 5 | 57 | 20 | 92 |
| 6 | 17 | 21 | 16 | 6 | 42 | 21 | 60 |
| 7 | 22 | 22 | 28 | 7 | 88 | 22 | 76 |
| 8 | 18 | 23 | 24 | 8 | 81 | 23 | 110 |
| 9 | 20 | 24 | 27 | 9 | 55 | 24 | 63 |
| 10 | 21 | 25 | 25 | 10 | 66 | 25 | 76 |
| 11 | 17 | 26 | 26 | 11 | 74 | 26 | 64 |
| 12 | 19 | 27 | 23 | 12 | 52 | 27 | 98 |
| 13 | 21 | 28 | 13 | 13 | 82 | 28 | 77 |
| 14 | 17 | 29 | 19 | 14 | 71 | 29 | 61 |
| 15 | 22 | 30 | 20 | 15 | 69 | 30 | 77 |
| STATISTICAL PARAMETERS | | | | | | | |
| N | 30 | | | 30 | | | |
| SUM | 639 | | | 2198 | | | |
| MEAN | 21.3 | | | 73.3 | | | |
| SD | 3.69 | | | 18.33 | | | |
| SEM | 0.67 | | | 3.35 | | | |
| CV | 17.13 | | | 25.03 | | | |
| Range | 13 – 28 | | | 42 – 121 | | | |
| Min | 13 | | | 42 | | | |
| Max | 28 | | | 121 | | | |
| 't' between | Degree of freedom | | 't' | 'p' | | | |
| A and B | 58 | | -15.23 | <0.001 | | | |

**Table 2** shows that the serum ADA values in the test group have been significantly increased with a mean +SD of 73.3+18.33 U/L in comparison to the control group with mean +SD of 21.3+3.69 U/L. The't' value is -15.23 and the 'P' value is <0.001.

**Liver function test in hepatitis**:
The mean serum total bilirubin level is more in test group (9.1 mg/dl) than that in control group (0.77 mg/dl). Mean serum AST level is more in the test group (544.6 U/L) than that in the control group (29.9 U/L). Mean serum ALT level is more in the test group (751.2 U/L) than that in the control group (33.6 U/L). Mean serum total protein level is decreased in the test group (6.42 g/dl) than that in the control group (7.29 g/dl). Mean serum albumin

level in the test group (3.42 g/dl) is decreased than that in the control group (4.44 g/dl).

**CORRELATION STUDIES**

a) Correlation between total bilirubin and ADA in hepatitis:

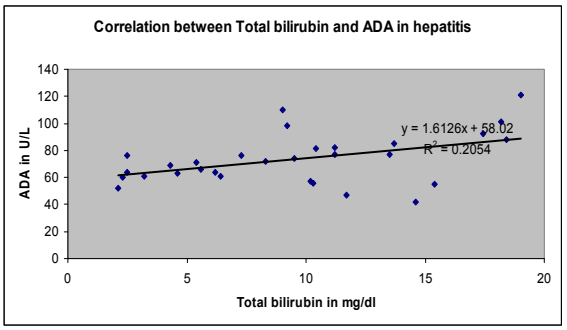


**Figure 2** shows that there is positive correlation between ADA and total bilirubin in hepatitis with correlation coefficient r = 0.4533 which is significant with P=0.0119 i.e <0.05

b) Correlation between AST and ADA in hepatitis:

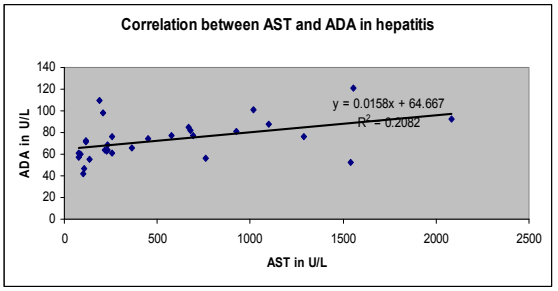


**Figure 3** shows that there is positive correlation between ADA and AST in hepatitis with correlation coefficient r=0.4563 which is significant with P=0.0113 i.e <0.05

c) Correlation between ALT and ADA in hepatitis:

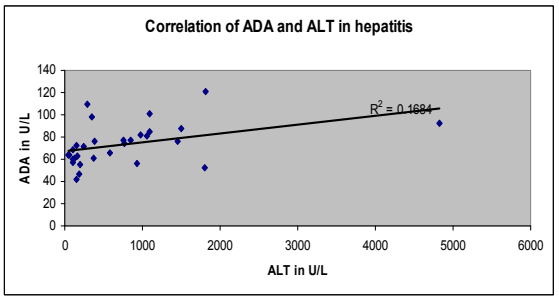


**Figure 4** shows that there is positive correlation between ADA and ALT in hepatitis with correlation coefficient r=0.4104 which is significant with P=0.0243, i.e. <0.05

Negative correlation have been found between ADA and albumin in hepatitis with correlation coefficient r= - 0.2539 and P>0.1, i.e., not significant. Similarly, there is no correlation between ADA and total protein in hepatitis with correlation coefficient r = 0.09198 and P>0.1, i.e., not significant.

## DISCUSSION

This study shows that, serum adenosine deaminase activity in hepatitis patients have a significantly higher value compared to the control subjects (p<0.001). The control group comprising of 30 individuals have a mean serum adenosine deaminase activity of 21.3+3.69. The test group consisting the same number of cases has a mean serum adenosine deaminase activity of 73.3+18.33 with a significance of P<0.001 against 58 degrees of freedom. So, the high values found in hepatitis against control group are statistically highly significant. This means that hepatitis patients have higher values of serum ADA against normal healthy individual. Kalkan A et al, 1999[12] in the study 'Adenosine Deaminase and Guanosine Deaminase Activities in Sera of Patients with Viral Hepatitis' stated that increase in serum ADA activities in hepatitis forms may be dependent on and reflect the increase in phagocytic activity of macrophages and maturation of T-lymphocytes, and may be valuable in monitoring in viral hepatitis cases. According to Kobayashi F et al, 1993[4] ADA activities are raised also in alcoholic hepatitis. Although in toxic and alcoholic hepatitis, there is no macrophage activity or lymphocyte proliferation, the raised serum ADA activity may be due to ADA1 isoenzyme which is because of the hepatocyte damage as described by Kurata N et al[13]. The result obtained matches with the results found by various authors like Takahashi M et al 1984[14], Wang J L et al 1986[15], Kaya S et al 2007[16], Vasudha K C et al 2006[17], Pratibha K et al 2004[18], etc.

Very highly significant differences in the liver function tests between the normal control and the test group with hepatitis shows that the levels of the liver function tests are significantly affected by the hepatocyte status under hepatitis and establishes the reliability for their comparative analysis with the secondary variable adenosine deaminase. In the present study, positive correlation was detected between the levels of ADA and those of ALT, AST and total bilirubin in hepatitis cases.

## CONCLUSION

From this small study, it can be concluded that serum ADA activity in hepatitis is significantly raised than that in the normal healthy persons. The serum ADA activity is increased with increasing levels of serum transaminases and total bilirubin levels.

To increase both the sensitivity and the specificity of laboratory tests in the detection of liver disease, it is best to use them as a battery. Testing for serum adenosine deaminase level in hepatitis gives us an idea about the mononuclear cell infiltration and lymphocytic proliferation that occurs in hepatitis along with hepatocyte damage. Inclusion of this test to identify the inflammatory reactions occurring in hepatitis will help in monitoring the clinical status of the hepatitis patient and hence the prognosis.

**Acknowledgement**: I am indebted to Dr. Putul Mahanta Sir for his valuable advice in miscellaneous aspects.

**Ethical clearance**: Taken

**Source of funding**: Nil

**Conflict of interest**: Nil

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