A STUDY OF SERUM ADENOSINE DEAMINASE LEVELS AND LIVER FUNCTION TESTS IN LIVER DISORDERS

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ABSTRACT

BACKGROUND

Aim of this study is to estimate serum adenosine deaminase activity and biochemical profile in various liver disorders.

MATERIALS AND METHODS

The present study included 50 cases of different categories of liver diseases and 25 controls. The liver disorders are divided into 5 categories. 1. Viral hepatitis (n=8) 2. Cirrhosis of liver (n=16) 3. Obstructive jaundice (n=10) 4. Tumours of liver (n=8) 5. Drug-induced jaundice (n=8).

RESULTS

ADA is significantly elevated in all the groups of liver diseases except Obstructive jaundice ($p < 0.0001$). AST significantly elevated in all the groups of liver diseases ($p < 0.01$). ALT and Serum Bilirubin are significantly elevated in all except Liver tumours ($p < 0.02$ & 0.0001). ALP is significantly elevated in all cases except Drug-induced jaundice ($p < 0.001$). Total serum proteins are significantly decreased only in Obstructive jaundice ($p < 0.0005$). Serum Albumin is significantly decreased in Cirrhosis of liver, Obstructive jaundice, and Tumours of liver ($p < 0.0001$). Serum Globulin levels are significantly elevated in Acute Hepatitis, Cirrhosis of liver and decreased in Obstructive jaundice ($p < 0.005$).

CONCLUSIONS

Serum ADA levels along with other liver enzymes estimation in the serum of patients serves as prognostic/diagnostic aid in the evaluation of liver disorders.

KEYWORDS

ADA: Adenosine Deaminase, SGOT: Serum Glutamate Oxaloacetate Transaminase, SGPT: Serum Glutamate Pyruvate Transaminase, ALP: Alkaline Phosphatase, Cell Mediated Immunity, Liver Diseases.

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BACKGROUND

A number of serum enzymes have been used to assess hepatocellular injury but they have limitations in sensitivity and specificity.

Liver plays a central role in maintenance of metabolic homeostasis, development of clinically important liver disease is accompanied by diverse manifestations of disordered metabolism.⁽¹⁾

Increased serum ADA activity has been observed in infectious diseases caused by micro-organisms infecting mainly the macrophages like tuberculosis, visceral and cutaneous leishmaniasis, brucellosis, typhoid fever and HIV infection.⁽²⁻⁵⁾

In the above disorders studied, ADA seems to originate exclusively from the monocyte/macrophage lineage and therefore reflects the involvement of cellular immune system.

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Hence, serum ADA along with other liver enzymes estimation in the serum of patients serves as prognostic/diagnostic aid in the evaluation of liver disorders.

The abnormality of liver function tests is particularly important in anicteric patients who may have unsuspected disorders such as viral hepatitis, chronic active hepatitis, cirrhosis or partial bile duct obstruction.

Once the presence of hepatic dysfunction is recognised, the pattern of laboratory test abnormalities may allow clinicians to recognise the general type of the liver disorder. To increase the sensitivity and specificity of laboratory tests, it is better to use them as a battery of tests.

Adenosine aminohydrolase (ADA) E.C.3.5.4.4 is an enzyme that catalyses deamination of adenosine forming inosine. It is an enzyme involved in catabolism of purine bases. Its principal activity is detected in T-lymphocytes owing to its higher presence in lymphoid tissues.

It is involved in lymphocytic proliferation and differentiation. It is a marker of cell mediated immunity, its activity is higher in diseases that elicit a cell mediated immune response.

Adenosine deaminase is a cytosolic enzyme, which is of considerable interest because in humans, a congenital defect

of the enzyme causes severe combined immunodeficiency (SCID).

Conway and Cooke were first to study the distribution of ADA in various organs of rabbit and humans. In humans, highest ADA activity is found in Thymus and other lymphoid tissues (Approx. 800 IU/mg), the lowest in erythrocytes (Approx. 1 IU/mg). Among the non-lymphoid tissues in humans, relatively high levels of ADA are found in the villi of epithelial cells lining the duodenum; levels are lower in other portions of the gastrointestinal tract.

The aim of the present study is to estimate Serum Adenosine deaminase activity along with liver function tests in various liver disorders and the objective is to assess the utility of the above parameter as diagnostic or prognostic indices of liver diseases.

MATERIALS AND METHODS

Total number of 50 Patients with a diagnosis of viral Hepatitis (n=8), Cirrhosis of liver (n=16), Obstructive Jaundice (n=10), Tumours of Liver (n=8), Drug-induced Jaundice (n=8) were selected for this study.

Inclusion Criteria

Patient population included adults aged from 20-60 years, in whom the diagnosis of the cases were confirmed by clinical features, pathological, serological and other radiological findings.

Exclusion Criteria

Patients with other diseases such as diabetes mellitus, cardiovascular diseases, hypertension, kidney disease were excluded from the study.

Age and sex matched 25 healthy subjects were taken as control group for this study.

Ethical consents were obtained from all participants of this study.

5 mL blood samples from both cases and controls were collected without addition of anticoagulant. Serum was separated and subjected for the estimation.

1. Serum Adenosine deaminase (Galanti & Giusti method).⁶
2. Serum aminotransferases-AST, ALT (Modified IFCC method).^{7,8}
3. Serum Alkaline phosphatase (King and King's method 1954).
4. Serum Total Bilirubin (Modified Jendrassik & Grof's method).⁹
5. Serum Total Proteins (Biuret method).¹⁰
6. Serum Albumin (Bromocresol green dye binding method).¹¹
7. Serum Globulins (Derived parameter).

Measurement of ADA based on spectrophotometric measurement of coloured indophenols complex from ammonia liberated from adenosine.

Liver enzymes, Bilirubin, Total protein, Albumin were quantitated with standard manufacturer kit assays using a fully automated Chemistry analyser.

Statistical Analysis

Was done using SPSS package, results were expressed as mean±S.D.

ADA, Total Bilirubin, Total protein, Albumin, liver enzymes of controls and cases were compared using student's t test.

RESULTS

The present study included 50 cases of liver diseases and 25 healthy individuals as control group in whom serum Adenosine deaminase, serum SGOT, SGPT, Alkaline phosphatase, serum total bilirubin, serum total proteins, serum albumins and globulins were estimated.

Sl. No.	Variables	Mean	S.D
1	ADA	21.08	4.55
2	ALT	26.48	7.96
3	AST	28.00	6.76
4	ALP	64.84	9.76
5	T. Bil	0.68	0.293
6	T. Protein	6.708	0.866
7	Albumin	4.1	0.427
8	Globulin	2.52	0.622

Table 1. Mean, S.D of all Parameters of Control Group

Sl. No.	Variable	Mean	S.D	P Value
1	ADA	79.13	10.72	<0.0001
2	ALT	278.25	537.16	0.0212
3	AST	166.50	265.12	0.0110
4	ALP	184	173.48	0.0013
5	T. Bil	8.575	5.503	<0.0001
6	T. Protein	7.125	0.763	0.2176
7	Albumin	3.925	0.727	0.3890
8	Globulin	3.200	0.334	0.0075

Table 2. Statistical Analysis of Cases of Acute Hepatitis

Sl. No.	Variable	Mean	S.D	P Value
1	ADA	38	18.33	0.0001
2	ALT	40.50	18.33	0.0020
3	AST	53.19	20.15	<0.0001
4	ALP	131.56	84.80	0.0003
5	T. Bil	2.038	1.793	<0.0005
6	T. Protein	6.113	0.949	0.0459
7	Albumin	2.769	0.784	<0.0001
8	Globulin	3.281	0.571	0.0005

Table 3. Statistical Analysis of Cases of Liver Cirrhosis

Sl. No.	Variable	Mean	S.D	P Value
1	ADA	47.50	26.98	<0.0111
2	ALT	123.25	75.64	<0.0001
3	AST	101.88	57.20	<0.0001
4	ALP	72	35.09	0.3546- not Significant
5	T. Bil	2.038	1.793	0.0010
6	T. Protein	6.338	1.277	0.3622- Not significant
7	Albumin	3.175	0.755	<0.0001
8	Globulin	3.037	0.632	0.0625

Table 4. Statistical Analysis of Cases of Drug-induced Jaundice

Sl. No.	Variable	Mean	S.D	P Value
1	ADA	22.30	26.98	0.4506- Not Significant
2	ALT	88.10	38.38	<0.0001
3	AST	96.20	82.38	<0.0001
4	ALP	24.930	196.06	<0.0001
5	T. Bil	6.35	5.67	<0.0001
6	T. Protein	5.40	1.06	0.0005
7	Albumin	3.27	0.79	0.0002
8	Globulin	2.01	0.66	0.0247

Table 5. Statistical Analysis of Cases of Obstructive Jaundice

Sl. No.	Variable	Mean	S.D	P Value
1	ADA	34.25	10.90	<0.0001
2	ALT	42.25	41.08	0.0706-Not Significant
3	AST	50.38	24.84	0.0002
4	ALP	143.63	33.89	<0.0001
5	T. Bil	0.875	0.410	0.1168-Not Significant
6	T. Protein	6.038	1.027	0.0776-No Statistical Significance
7	Albumin	2.850	0.746	<0.0001
8	Globulin	3.063	0.936	0.0826

Table 6. Statistical Analysis of Cases of Liver Tumours

DISCUSSION

Present study was categorised into 5 groups of liver diseases and are discussed by liver disorder type, parameter wise.

Acute Hepatitis- (N=8)

Serum ADA, Alanine transaminase, Aspartate transaminase, Alkaline phosphatase, Serum total bilirubin, Serum globulin showed significant elevation compared to controls.

These findings are in agreement with past studies of Ahmed Kalkan et al 1999,⁽¹²⁾ K. Pratibha et al 2004,⁽¹³⁾ Selcuk Kaya et al 2007.⁽¹⁴⁾

Serum total proteins are not significantly varied (p value=0.2176) with a mean value of 7.125 ± 0.763 compared to controls 6.70 ± 0.86 .

Serum albumin showed no variation in values (p value=0.3890) with a mean value of 3.925 ± 0.727 compared to controls 4.10 ± 0.42 .

In infectious hepatitis, steep rise in serum ADA levels occur as a result of lipid peroxidation of membrane lipids.

In the first phase of infective hepatitis, the host cells mount an immune response by production of leukocytes. Free radicals are released from activated leukocytes which cause peroxidation of membrane lipids.

Lipid peroxidation is followed by loss of structural integrity of plasma membranes thereby releasing the membrane associated enzymes like Adenosine deaminase and 5'-nucleotidase into the circulation.

Cirrhosis of Liver- (N=16)

Serum Adenosine deaminase levels showed significant elevation (p value <0.0001) with a mean value of 38.00 ± 18.33 , compared to controls 21.08 ± 4.55 .

Alanine transaminase levels showed significant elevation (p value=0.0020) with a mean value of 40.50 ± 18.33 , compared to controls 26.48 ± 7.96 .

Aspartate transaminase values also showed significant elevation (p value <0.0001) with a mean value of 53.19 ± 20.15 , compared to controls 28.00 ± 6.76 .

Alkaline phosphatase levels showed significant elevation (p value=0.0003) with a mean value of 131.56 ± 84.80 , compared to controls 64.84 ± 9.75 .

These findings are in agreement with past studies of D.M Goldberg et al 1965,¹⁵ Pace M, Dotta C et al 1990,¹⁶ Sheila Sherlock and J Dooley 1993¹⁷ and Sanjiv Chopra et al 1985.¹⁸

Serum Total Bilirubin values showed highly significant elevation (p value <0.0005) with a mean value of 2.038 ± 1.793 , compared to controls 0.66 ± 0.30 .

Serum Total proteins showed no variation (p value=0.0459) with a mean value of 6.113 ± 0.949 , compared to controls 6.70 ± 0.86 .

Serum Albumin showed highly significant decrease in values (p value <0.0001) with a mean value of 2.769 ± 0.784 , compared to controls 4.10 ± 0.42 .

Serum globulin showed significant elevation (p value=0.0005) with a mean value of 3.281 ± 0.571 , compared to controls 2.56 ± 0.64 .

Drug-induced Jaundice (N=8)

Serum Adenosine deaminase levels, Alanine transaminase levels, Aspartate transaminase values, Serum Total Bilirubin values showed significant elevation compared to controls.

Serum Alkaline phosphatase levels, Serum Total proteins, Serum globulin showed no statistical significance.

The findings of my present study were compared with past study of D.M Goldberg et al 1966.¹⁵

Serum Albumin showed highly significant decrease in values (p value <0.0001) with a mean value of 3.175 ± 0.755 , compared to controls 4.10 ± 0.42 .

In Drug-induced jaundice, high serum ADA levels were observed in patients with hepatitis following administration of para-amino salicylic acid.

Obstructive Jaundice (N=10)

Serum Adenosine deaminase levels showed no statistical significance (p value=0.4506) with a mean value of 22.30 ± 26.98 compared to controls 21.08 ± 4.55 . Alanine transaminase levels showed significant elevation (p value <0.0001) with a mean value of 88.10 ± 38.38 , compared to controls 26.48 ± 7.96 .

Aspartate transaminase values also showed significant elevation (p value <0.0001) with a mean value of 96.20 ± 82.38 , compared to controls 28.00 ± 6.76 .

Alkaline phosphatase levels showed significance elevation (p value <0.0001) with a mean value of 249.30 ± 196.06 , compared to controls 64.84 ± 9.75 .

These findings are in agreement with past studies of D.M Goldberg et al 1965,¹⁵ Sheila Sherlock and J Dooley 1993,¹⁷ Sanjiv Chopra et al 1985.¹⁸

Serum Total Bilirubin values showed highly significant elevation (p value <0.0001) with a mean value of 6.35 ± 5.67 , compared to controls 0.66 ± 0.30 .

Serum Total proteins showed highly significant decrease in values (p value=0.0005) with a mean value of 5.40 ± 1.06 , compared to controls 6.70 ± 0.86 .

Serum Albumin showed highly significant decrease in values (p value=0.0002) with a mean value of 3.27 ± 0.79 , compared to controls 4.10 ± 0.42 .

Serum globulin showed significantly decreased values (p value=0.0247) with a mean value of 2.01 ± 0.66 , compared to controls 2.56 ± 0.64 .

Liver Tumours (N=8)

Serum Adenosine deaminase levels showed significant elevation (p value <0.0001) with a mean value of 34.25 ± 10.90 compared to controls 21.08 ± 4.55 .

Alanine transaminase levels showed no statistical significance (p value=0.0706) with a mean value of 42.25 ± 41.08 , compared to controls 26.48 ± 7.96 .

Aspartate transaminase values also showed significant elevation (p value=0.0002) with a mean value of 50.38 ± 24.84 , compared to controls 28.00 ± 6.76 .

Alkaline phosphatase levels showed highly significant elevation (p value <0.0001) with a mean value of 143.63 ± 33.89 , compared to controls 64.84 ± 9.75 .

These findings are in agreement with past studies of D.M Goldberg et al 1965,¹⁵ Sheila Sherlock and J Dooley 1993,¹⁷ Sanjiv Chopra et al 1985.¹⁸

Serum Total Bilirubin values showed no statistical significance (p value=0.1168) with a mean value of 0.875 ± 0.410 , compared to controls 0.66 ± 0.30 .

Serum Total protein values showed no statistical significance (p value=0.0776) with a mean value of 6.038 ± 1.027 , compared to controls 6.70 ± 0.86 .

Serum Albumin showed decreased values which are highly significant (p value<0.0001) with a mean value of 2.850 ± 0.746 , compared to controls 4.10 ± 0.42 .

Serum globulin values showed no statistical significance (p value=0.0826) with a mean value of 3.063 ± 0.936 , compared to controls 2.56 ± 0.64 .

Slightly higher levels of ADA were observed in Hepatomas when compared to Liver secondaries.

CONCLUSIONS

From the data presented above, it is clear that serum ADA activity is increased in all cases of acute hepatitis, moderately increased in cases of hepatic cirrhosis, drug-induced jaundice and liver tumours. There was no increase in serum ADA activity in cases of obstructive jaundice (Simple cholelithiasis).

Serum adenosine deaminase estimation is simple and can be performed even in a less equipped laboratory. This facilitates wider usage of this assay as a diagnostic/prognostic tool for the cases of viral hepatitis, also aid in the differential diagnosis of liver disorders.

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