Original article:

Serum adenosine deaminase levels in hepatic disorders

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Abstract:

The diagnosis of organ disease is aided by measurement of number of nonfunctional plasma enzymes characteristic of that organ/tissue. The amount of enzymes released depends on the degree of cellular damage, the intra-cellular concentration of enzymes, and the mass of the effected tissue. The concentration of enzyme released reflects the severity of damage. Once the presence of hepatic dysfunction is recognized the pattern of laboratory test abnormalities may allow clinicians to recognize hepato cellular disorders such as viral hepatitis from cholestatic such as primary cirrhosis and bile duct obstruction. ADA activity was first noticed by Gyori and Rothler. The enzyme is widely distributed and is found in intestinal mucosa, spleen, liver, skeletal muscle, kidney, serum, lymphocytes, leukocytes, erythrocytes. Adenosine deaminase is an enzyme involved in purine metabolism and its physiological role is related to lymphocytic proliferation and differentiation. Serum adenosine immune response.

In conclusion, it is clear that ADA activity is increased in all cases of acute hepatitis and moderately increased in cases of hepatic cirrhosis, drug induced jaundice and liver tumors. There is no increase in ADA in cases of obstructive jaundice. Adenosine deminase estimation serve to diagnose the patients with infective hepatitis in the initial stages along with liver function tests and also aid in differential diagnosis of liver diseases.

Introduction:

The almost universal availability of automated biochemical analysis and the Influence of insurance, employment and health screening examinations had led increasingly to the identification of abnormal biochemical liver tests in asymptomatic people. To increase the sensitivity and specificity laboratory tests it is best use them as battery of test.

The diagnosis of organ disease is aided by measurement of number of nonfunctional plasma enzymes characteristic of that organ/tissue. The amount of enzymes released depends on the degree of cellular damage, the intra-cellular concentration of enzymes, and the mass of the effected tissue. The concentration of enzyme released reflects the severity of damage. Mild inflammatory conditions are likely to release cytoplasm enzymes whereas necrotic conditions release mitochondrial enzymes as well. The use of an appropriate abnormal range is important in evaluating abnormal levels of plasma enzymes.

The estimation adenosine deaminase activity in liver serves as prognostic aid in evaluation of liver disorders. The liver functions provide a sensitive noninvasive method for method sereening for the presence of liver dysfunction. This is particularly important in anicteric patients who may have unsuspected disorders such as viral hepatitis, Chronic active hepatitis or cirrhosis.Once the presence of hepatic dysfunction is recognized the pattern of laboratory test abnormalities may allow clinicians to recognize hepato cellular disorders such as viral hepatitis from cholestatic such as primary cirrhosis and bile duct obstruction.

ADA activity was first noticed by Gyori and Rothler. The enzyme is widely distributed and is found in intestinal mucosa, spleen, liver, skeletal muscle, kidney, serum, lymphocytes, leukocytes, erythrocytes.Adenosine deaminase is an enzyme involved in purine metabolism and its physiological role is related to lymphocytic proliferation and differentiation. Serum adenosine immune response.

The aim of present study is to estimate serum adenosine deaminase activity in patients with different liver disorders and the objective is to assess the utility of the above parameter as diagnostic or prognostic indices or liver function and in addition the liver function tests estimated in he study include serum concentrations of amino transferase (ALT&AST), Alkaline phosphatases, Total bilirubin in various in various liver disorders like acute and chronic parenchymal liver diseases, obstructive jaundice, hepto cellular carcinoma.

Materials and methods:

1.ESTIMATION OF SERUM ADA ACTIVITY BY GALANTI and GIUSTI 1965

2.ESTIMATION OF AMINO TRANSFERASES (ALT AND AST BY REITMAN AND FRANKEL 1957)

3.ESTIMATION OF SERUM BILIRUBIN BY MELOY AND EVELYM IN 1937

4.ESTIMATION OF ALKALINE PHOPHATASE BY KING AND KINDS METHOD, 1954

Results:

The present study included 25 cases of liver diseases and 15 individials as control group in whom Adenosine deaminase, serum ALT, AST, Alkaline phosphatase, serum total bilirubin were estimated . Present study was categorized in to 5 groups according to diseases of the table as per results obtained discuesed parameter wise.

Table:1 study of control group various parameter values mean, sd, sem of control group:

S.NO	VARIABLES	MEAN	S.D	SEM
1	ADA	21.07	4.367	1.127
2	ALT	27.07	8,102	2.09
3	AST	28.33	6,091	1.573
4	AKP	64.8	9,571	2.471
5	Sr.Bil	0.65	0.294	0.076

The Mean, S.D, S.E.M of Serum Adenosine deaminase, Liver enzymes (A.L.T.A.S.T,A.K.P), Serum Bilirubin of in control groups are represented in table-The are with in the established normal values.

Table: 2 study cases of liver disorders statistical analysis of drug induced jaundice:

S.NO	VARIABLES	MEAN	S.D	SEM	P VALUE
1	ADA	47.6	15.71	7.026	<0.0001
2	ALT	123.0	48.29	21.59	<0.0001
3	AST	102.2	61.0	27.28	<0.0001
4	AKP	72.2	36.70	16.41	0.478 Not significant
5	Sr.Bil	3.9	2.62	1.17	0.0001

Serum adenosine deaminase, SGPT,SGOT,Serum Bilirubin levels are found to higher, when compared to controls

Table: 3 statistical analysis of CSES of acute hepatitis:

S.NO	VARIABLE	MEAN	S.D	SEM	P VALUE
1	ADA	79.20	105.92	4.73	<0.0001
2	ALT	142.4	69.78	31.21	<0.0001
3	AST	98.2	55.22	24.69	0.0001
4	AKP	223.4	163.9	73.305	0.0009
5	Sr.Bil	8.44	5.05	2.261	<0.0001

Serum Adenosine deaminase, serum Alanine serum Alanine transaminase, serum Aspartate transaminase, Alkaline phosphatase, Serum total Bilrubin levels found to be elevated when compare to controls

Table: 4 statistical analyses of cases of cirrhos of liver:

S.NO	VARIABLES	MEAN	S.D	SEM	P VALUE
1	ADA	38.0	12.7	5.673	0.0002
2	ALT	40.8	16.36	7.317	0.0193
3	AST	53.4	26.50	9.168	<0.0001
4	AKP	129.8	34.75	15.542	0.0003
5	Sr.Bil	2.04	1.842	0.823	0.0083

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Serum Adenosine deaminase, serum Alanine transaminase, serum Aspartate transaminase, Alkaline phosphotase, Serum total Bilirubin levels found to be elevated when compare to controls.

Table: 5---statistical analysis of cases of liver tumors:

S.NO	VARIABLES	MEAN	S.D	SEM	P VALUE
1	ADA	36	9.77	4.37	<0.0001
2	ALT	49	48.9	21.9	0.0903, Not Significant
3	AST	54	20.1	8.98	0.0002
4	AKP	142	39.23	17.54	<0.0001
5	Sr.Bil	0.86	0.6148	0.275	0.3135, not significant

Serum Adenosine deaminase, serum Aspartate transaminase, Alkaline phosphotase, levels found to be elevated Serum. Alanine Transaminase, Total Bilirubin levels show no variation when compared to controls.

Table:6---statistical analysis of cases of obstructive jaundice:

S.NO	VARIABLES	MEAN	S:D	SEM	P VALUE
1	ADA	22.2	3.271	1.463	0.603,7 Not significant
2	ALT	92.2	52.78	23.603	<0.0001
3	AST	88.2	46.31	20.7	<0.0001
4	AKP	249.6	194.7	98.8	0.0125
5	Sr.Bil	6.306	5.47	2.447	0.0004

Serum Adenosine deaminase, levels show no variation. Serum Aspartate transaminase, Alkaline phosphotase, Alanine transaminase, Total Bilirubin levels found to be elevated serum when compared to control.

Discussion:

1) Acute hepatitis : (N=5):

a) Serum adenosine deaminase level showed significant elevation (p value<0.0001) with mean value of 79.13±10.59 compare to control 21.08+4.36

b) Alanine transaminase showed significant elevation (p value=0.001) with mean value of 142.4±69.78 compared to controls 27s.07±8.4.36

c) Aspartate transaminase vaules also showed significant elevation (p value<0.001) with mean value 98.33±50.2 of compared to controls 28.33±6.09

d) Alkaline phosphatase values also showed significant elevation (p value=0.0009) with mean value 223.4±163.0 of compared to controls 64.4±9.57

e) Serum total bilirubin values also showed highly significant elevation (p value<0.0001) with mean value 8.44±5.05 of compared to controls 0.65±0.294.

These findings are in agreement with past studies of K. Prathiba et al 2004, selcuk kaya et al 2007 shown in the table

S.no	Name the study	Biochemical findings
1	K.Pratibha, usha anand etal 2004	SAD-significantly elevated (p value <0.005) AST,ALT significantly elevated (p value <0.001)1 AKP- not statistically significant (p value>0.05 S.T.bilurubin statistically significant (p value<0.0010
2	Selcuk kaya, Emel sesli, caal et al 2007	SAD-significantly elevated (p value <0.001) AST,ALT significantly elevated (p value <0.05)
3	Present study 2008	SAD-significantly elevated (p value <0.001) ALT-significantly elevated (p value=0.02) AST-significantly elevated (p value =0.01) AKP-significantl elevated (p value =0.001) S.T.bilurubin significantly elevated (p value<0.001)

2) CIRRHOSIS OF LIVER(N=5):

a) Serum adenoine deaminase level showed significant elevation (p value=o.0002) With mean value of 38.0±12.7 compare to control 21.08±4.367

b) Alanine transaminase showed significant elevation)p value=0.0193) with mean value of 40.8±16.36 compared to controls 27.07±8.10.2015

c) Aspartate transaminase values also showed significant elevation (p value <0.0001) wih mean value 53.4±20.50 of compared to controls 28.33±6.09

d) Alkaline phosphatase values also showed significant elevation (p value=0.003) with mean value 129.8±34.75 of compared to controls 64.8±9.57

e) Serum total bilirubin values also showed highly significant elevation (p value =0.0083) with mean value 2.04±1.84 of compared to controls 0.65±0.29.

These findings are in agreement with past studies of D.M. Goldberg 1965, Pace m Dotta c et al 1990 Sheila and Sherlock and J Dooley 1993 shown in the table.

s.no	Name the study	Biochemical findings
1	D.M.Goldberg 1965	SAD,AST,ASLT,S.Bil- Significantly elevated
2	Pace m Dotta c et al 1990	AST,ALT,AKP – Significantly elevated
3	Sheila and Sherlock and Dooley 1993	AST,ALT – highly Significantly AKP,S.Bil significantly elevated
4	Present sudy	SAD, AST, ASLT,S.Bil- Highly Significantly increase

3) Drug induced jaundice:

a) Serum adenosine deaminase level showed significant elevation (p value< 0.0001) With mean value of 47.6±15.7 compare to control21.08±4.36

b) Alanine transaminase showed significant elevation (p value<0.0001) with mean value of 123±48.29 compared to controls 27.07±8.10.2015

c) Aspartate transaminase values also showed significant elevation (p value 0.0001) with mean 102.2±61.0 value of compared to controls 28.33±6.09

d) Alkaline phosphatase values showed no significance (p value=0.478) with mean value of 72.2±36.7 compared to controls 64.8±9.57

e) Serum total bilirubin values also showed significant elevation (p value<0.001) with mean 2.7±1.63 value of compared to controls 0.65±0.29

These findings are in agreement with past studies of D.M.Goldberg 1965.

s.no	Name the study	Biochemical findings
1	D.M.Goldberg 1965	SAD,ALT,AST,S.Bil- Significantly elevated
2	Present study	SAD,ALT,AST,S.Bil- Significantly elevated AKP not significant

4) Obstructive jaundice(N:5):

a) Serum adenosine deaminase level shows no statistical significance (p value =0.6037) With mean value of 22.2±3.27 compare to control 21.08±4.367

b) Alanine transaminase showed significant elevation (p value=0.001) with mean value of 92.2±52.7 compared to controls 27.07±8.10.2015

c) Aspartate transminase values also showed significant elevation (pvalue<0.0001) with mean 88.2±46.3 value of compared to controls 28.33±6.09

d) Alkaline phosphatase values showed significance elevations (p value<0.00125)with mean 249.6±194.7 value of compared to controls 64.8±9.57

e) Serum total bilurubin values showed highly significant elevation (p value0.0004) with mean 6.38±5.47 value of compared to controls 0.65±0.29

These findings are in agreement with past studies of D.M.Goldberg 1965, Sheila Sherlock and Dooley 1993, Sajiv chopra etal 1985, shown

s.no	Name of study	Biochemical findings
1	Sheila and Sherlock and Dooley 1993	ALT,AST,AKP,S.Bil- Significantly elevated
2	Sheila and Sherlock and J Dooley 1993	ALT,AST,AKP,S.Bil significantly elevated
3	Sanjiv chopra, Patric H Griffin 1985	ALT, S.Bil significantly elevated
4	Present study	ALT,AST,S.Bil- highly Significant,AKP significantly elevated

5) Liver tumours (N:5)

a) Serum adenosine deaminase level showed significant elevation (p value <0.001)With mean value of 36.0±9.77 compare to control 21.08±4.36

b) Alanine transaminase showed no stasistical significant (p value=0.0903) with mean value of 49.2±48.9 compared to controls 27.08±4.36

c) Aspartate transaminase values also showed significant elevation (value=0.0002) with mean 54±20. 1 value of compared to controls 28.33±6.09

d) Alkaline phosphatase values shows highly significance (p value<0.001) with mean value of 142.1±39.23 compared to controls 64.8±9.57

e) Serum total bilurubin value shows not statistical significant (p value=03135) with mean value of 0.86±0.61 compared to controls 0.65±0.29

These findings are in agreement with pat studies of D.M.Goldberg 1965, Sheila Sherlock and Dooley 1993, Sajiv chopra etal 1985, shown

s.no	Name the study	Biochemical findings
1	D.M.Goldberg 1965	SAD,AST- Significantly elevated
2	Sheila and Sherlock and J Dooley 1993	ALT,AST- significantly AKP-highly Significant S.Bil ignificantly elevated
3	Sanjiv chopra, Patric Griffin 1985	AKP-highly significant
4	Present study	SAD,AKP,AST- Significantly elevated ALT,S.Bil-not significant

From the data presented above, it is clear that SAD activity is increased in all cases of acute hepatitis, three quarters of the cases of hepatic cirrhosis and half cases of drug jaundice and liver tumorous. There was no increase in SAD in cases of obstructive jaundice.

In above liver disorder studied SAD seems to originate exclusively from the monocyte/macrophage lineage and therefore reflects he involvement of cellular immune system. In acute lymphoblastic leukaemia, lymphoblasts are apparently the source of increased SAD. In infectious hepatitis, steep rise in SAD levels occur as a result of lipid peroxidation of membrane lipids, In the first phase adenosine deaminase into circulation.

Barnes etal (1995) reported that adenosine could lessen the potentially damaging activity of neutrophils at the site of infections. On other hand, ADA activity counter acts with adenosine by utilizing it. Therefore, development of some ADA inducer drugs or its direct administration ma be studies in future to lessen the risk of chronic liver disease due to hepatitis. In drug induced jaundice high SAD levels were given by patients with hepatitis following administration of Para immune salicylic acid.Slightly higher levels of SAD were observed in hepatomas when compared to liver secondaries. The levels of enzymes in T-lymphocytes vary according to cellular differentiation. The evidence of high SAD activity during rapid stimulated growth of normal tissues is of importance in making full functional purine salvage possible.

Serum adenosine deaminase is sensitive to stimulation b growth factors and cytokines during rapid tissue proliferation.The activity of ADA is increased in very rapidly growing malignancies while slow growing, well differentiated timorous do not express. Adenosine deamiase inhibitor (deoxcoformycin) resulted in inhibition of cell growth. This shows ADA plays important role in rapid growth of tissues by reutilization of nucleotides which are required for RNA and DNA syntiesis.

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Estimation serum bilirubin is routinely carried out in patients with liver disease as a diagnostic or prognostic index. Recent studies hav shown that bilirubin should not be considered as just a metabolic waste product; it function invivo as powerful antioxidant, antimutagen, anticomplement and an endogenous tissue protector.

Conclusion:

In conclusion, it is clear that ADA activity is increased in all cases of acute hepatitis and moderately increased in cases of hepatic cirrhosis, drug induced jaundice and liver tumors. There is no increase in ADA in cases of obstructive jaundice. Adenosine deminase estimation serve to diagnose the patients with infective hepatitis in the initial stages along with liver function tests and also aid in differential diagnosis of liver diseases.

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