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Original article

Evaluation of Serum Adenosine Deaminase Activity in Viral Hepatitis

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ABSTRACT

The evaluation of serum Adenosine deaminase in viral hepatitis patients may be considered a useful tool in monitoring clinical status of the disease. In this study serum ADA activity was estimated in viral hepatitis patients along with total bilirubin and liver enzymes. Materials and methods: 50 viral hepatitis patients (25males & 25 females) and 50 controls (25males & 25 females) were enrolled in the study. Adenosine deaminase, total bilirubin and liver enzymes were analyzed in both groups. Results: Adenosine deaminase levels were significantly increased in cases of Viral hepatitis compared to controls. Conclusion: We suggest that serum ADA levels are increased in Viral hepatitis patients. In the treatment of Viral hepatitis serum ADA levels should be considered a useful tool for monitoring liver condition.

1.Introduction:

Viral hepatitis is almost always caused by one of the hepatitis viruses HAV, HBV, HCV, HDV, HEV and non A, B, C, D, E [1]. Hepatitis can be described as an inflammatory process in the liver characterized by diffuse or patchy hepatocellular necrosis affecting all acini. Both viral and host factors are believed to be implicated in pathogenesis of hepatitis. Immune responses of the viruses could result in liver lesions [2]. CD4+ (T helper) and cytotoxic T cells produce cytokines which cause damage of liver in infected patients [3].

Since liver plays a central role in maintenance of metabolic homeostasis, development of clinically important liver disease is accompanied by diverse manifestations of disordered metabolism [4]. Liver has considerable functional reserve hence damage to liver may not affect its activity in total. Simple tests of liver function become insensitive indicators of liver diseases [5]. Diagnostic information thus provided by liver function tests is limited. Aminotransferases and viral load levels are usually used to monitor Viral hepatitis [6]. PCR quantitates viral load and is a reliable indicator of disease status [7].

Adenosine deaminase (ADA) catalyzes deamination of adenosine forming inosine. It is an enzyme involved in catabolism of purine bases [8, 9]. Its principal activity is detected in T lymphocytes owing to its higher presence in lymphoid tissues [10]. It is involved in lymphocytic proliferation and differentiation. As it is a marker for cell mediated immunity its activity is higher in diseases that elicit a cell mediated immune response [11, 12]. The evaluation of ADA activity in sera of hepatitis patients can thus be considered a useful marker in diagnosing hepatitis. Main aim of our study is to evaluate serum Adenosine deaminase in patients of viral hepatitis and the objective is to assess its utility as diagnostic or prognostic use.

2. Materials and Methods

2.1. Subjects

Subjects were 50 (25 male+25 female) patients in the age group of 20-50 years. As a control group 50 (25 male+25 female) healthy individuals aged 20-50 years from the same area were recruited. Ethical consents were obtained from all participants of this study. Clinical diagnosis was confirmed based on clinical symptoms, pathological, serological and radiological findings. 5ml blood samples from both cases and controls were collected without addition of anticoagulant. Serum was separated and subjected for the estimation of Serum Adenosine deaminase, total bilirubin and liver enzymes which included aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase(ALP) and lactate dehydrogenase(LDH).

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2.2. Measurement of serum ADA activity

Serum ADA activity was determined at 37ºC by a method described by Guisti and Galanti [13] which is based on Berthelot reaction. It is based on spectrophotometric measurement of colored indophenols complex from ammonia liberated from adenosine. The results are expressed in U/L. Normal range of ADA in healthy subjects is 4-20U/L.

2.3. Measurement of total bilirubin

Serum total bilirubin levels were measured Malloy and Evelyn method.

2.4. Measurement of liver enzymes

Enzymes required for evaluating liver function which included aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) were quantitated by using colorimetric techniques with kit assay systems in auto analyzer system. These were performed as described by manufacturers.

2.5. Statistical analysis

Statistical analysis was done using SPSS package. Results were expressed as mean ± Standard deviation (SD). ADA, total bilirubin and liver enzymes of cases were compared with controls by student's t test. Comparison of parameters in cases was done using One-Way ANOVA followed by post-hoc test.

3. Results

Table 1 shows mean and SD of all parameters studied in controls and viral hepatitis patients. ADA, bilirubin, AST, ALT, LDH were significantly ($p<0.05$) higher in viral hepatitis patients as compared to controls.

Table 1: Mean ± SD & p value of all parameters in controls and Viral hepatitis patients

Parameter	Controls	Cases	P Value
ADA	15.30 ± 2.23	66.56 ± 9.93	< 0.001
TOTAL BILIRUBIN	0.62 ± 0.23	10.71 ± 5.35	< 0.001
AST	20.00 ± 8.30	90.38 ± 32.83	< 0.001
ALT	22.20 ± 6.82	785.97 ± 399.33	< 0.001
ALP	17.43 ± 3.18	25.45 ± 2.45	> 0.05
LDH	321.47 ± 46.32	95.03 ± 24.91	< 0.001

According to Tables 2 & 3, Serum ADA activity did not vary significantly with age or gender. This will rule out the affect of age and gender on ADA levels and total significance can be attributed to the disease process itself.

Table 2: Mean ± SD of ADA according to age distribution in cases & controls

Subjects	21-30 years	31-40 years	>41 years
CONTROLS	14.85 ± 2.21	16.00 ± 2.12	15.28 ± 2.49
CASES	63.95 ± 10.95	56.62 ± 19.39	50.36 ± 24.75

Table 3: Mean ± SD of ADA according to gender

Subjects	Mean ± SD in CONTROLS	Mean ± SD in CASES
MALES	14.35 ± 1.58	64.85 ± 9.34
FEMALES	16.38 ± 2.4	59.67 ± 18.45

4. Discussion

Viral hepatitis has a high global prevalence. Its clinical course is also complicated and the available antiviral therapies are also not effective [14, 15]. Among all hepatitis infections B & C are most common and according to estimation by WHO 350 and 170 million people are infected worldwide with HBV & HCV respectively.

The first phase in infective hepatitis is the entry of virus into the parenchymal cells of liver. This is followed by an immune response of the host cell and infiltration of infected host cell by leukocytes. Severity and clinical outcome of hepatitis are controlled by the duration of illness before the initiation of appropriate therapy. Hence early diagnosis and initiation of therapy are important in decreasing the morbidity and mortality due to hepatitis.

A number of serum enzymes have been used to assess hepatocellular injury but they have limitations in sensitivity and specificity. In the present study we observed significant increase in serum ADA activity in viral hepatitis cases when compared to controls. We also have compared the ADA values according to the age and gender of cases and controls and observed that the variation was not statistically significant. Hence total significance can be attributed to the disease process itself.

Increased serum ADA activities have been observed in infectious diseases caused by microorganisms infecting mainly the macrophages like tuberculosis, visceral and cutaneous leishmaniasis, brucellosis, typhoid fever and human immunodeficiency virus infection [16-20].

The elevated serum ADA activity in hepatitis reflects phagocytic activity of macrophages and may provide useful additional diagnostic information on the pathogenesis of hepatitis.

Adenosine has a role in regulating inflammation as its increase diminishes inflammation [21, 22]. Literature is available on anti inflammatory action of systemic administration of adenosine. Adenosine decreases potentially damaging activity of neutrophils at the site of infections [23, 24].

5.Conclusion

The increase in serum ADA activities in hepatitis forms may be dependant on and reflects the increase in phagocytic activity of macrophages and maturation of T-lymphocytes and may be valuable in monitoring viral hepatitis cases. ADA test is simple and can be performed in even a less equipped laboratory. This facilitates wider usage of its assay as a diagnostic and prognostic tool.

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