

A STUDY OF HB A1C, ALANINE TRANSAMINASE (ALT), ASPARTATE TRANSAMINASE (AST) AND ALKALINE PHOSPHATASE (ALP) LEVELS IN ACUTE AND CHRONIC LIVER DISEASESS. Narasimha Rao Babji¹, M. Santhisree²**HOW TO CITE THIS ARTICLE:**

S. Narasimha Rao Babji, M. Santhisree. "A Study of Hb A1c, Alanine Transaminase (ALT), Aspartate Transaminase (AST) and Alkaline Phosphatase (ALP) levels in Acute and Chronic Liver Diseases". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 17, April 28; Page: 4473-4479, DOI: 10.14260/jemds/2014/2461

ABSTRACT: There are acute and chronic forms of hepatitis, which may result in nausea, jaundice, fatigue and abnormal liver function blood tests. Acute hepatitis is characterized by the parenchymal liver damage by any agent on an underlying normal liver which produces similar clinical and biochemical features. Chronic hepatitis is defined as hepatic necro- inflammation continuing for more than 6 months. Liver disease is often associated with an increased prevalence of impaired glucose tolerance and diabetes mellitus. The effect of HbA1c on Acute and Chronic liver diseases is not well studied. The present study is to know whether acute and chronic liver diseases have same effect on HbA1c or different effects on HbA1c and also to know the enzyme levels (ALT, AST and ALP) in these cases. **OBJECTIVES:** To study the effect of Acute Liver Disease and Chronic Liver Disease on Glycated hemoglobin (HbA1c), Alanine transaminase (ALT), Aspartate transaminase (AST) and alkaline phosphatase (ALP) levels. **METHODS:** A total number of 80 patients diagnosed and treated by Medical Department were taken for the study. Out of 80 patients, acute liver disease patients were 40 and Chronic liver disease patients were 40. Forty people who are age and sex matched, apparently healthy normal subjects were also studied as controls. Samples were analyzed for HbA1c, Alanine Transaminase (ALT), Aspartate transaminase (AST) and alkaline phosphatase (ALP). **Statistical analysis:** It is case control study. Analysis was done by Student's 't' test using Grphpad software. **RESULTS:** HbA1c values of acute liver disease shows no statistical significance when compared with controls. But HbA1c of Chronic liver disease shows statistical significance when compared with control. ALT, AST and ALP values of acute liver disease and chronic liver disease when compared with control shows very high significance. **CONCLUSION:** Chronic liver disease group shows significant increase in HbA1C when compared with control group, which may be due to endogenous insulin resistance which causes impaired glucose tolerance. Chronic liver disease has significant impact on hepatic glucose metabolism. ALT, AST and ALP values of Acute and Chronic liver diseases increased and show very high significance due to Liver disease and biliary obstruction in certain cases. **KEYWORDS:** Glycated hemoglobin (HbA1c), Alanine transaminase (ALT), Aspartate transaminase (AST) and alkaline phosphatase (ALP).

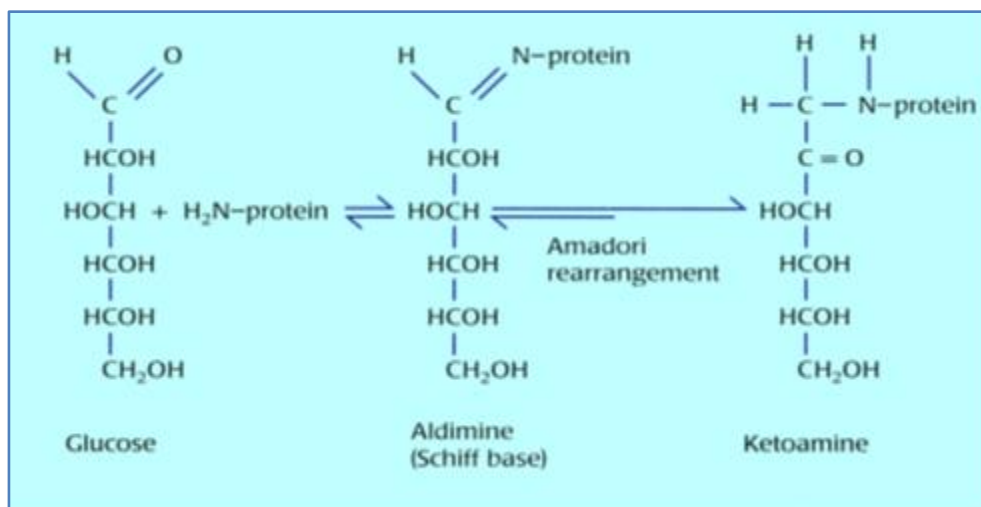
INTRODUCTION: Hepatitis is a nonspecific term for inflammation of the liver. There are acute and chronic forms of hepatitis, which may result in nausea, jaundice, fatigue and abnormal liver function blood tests. Acute hepatitis is characterized by the parenchymal liver damage by any agent on an underlying normal liver which produces similar clinical and biochemical features. It can be caused by viral infections, non-viral infections, drugs, toxins, alcohol, metabolic diseases and ischemia. Acute viral hepatitis is a systemic infection affecting the liver predominantly.

Almost all cases of acute viral hepatitis are caused by one of five viral agents: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), the HBV-associated delta agent or hepatitis D virus (HDV), and hepatitis E virus (HEV). All these human hepatitis viruses are RNA viruses, except for hepatitis B, which is a DNA virus. Although these agents can be distinguished by their molecular and antigenic properties, all types of viral hepatitis produce clinically similar illnesses. These range from asymptomatic and inapparent to fulminant and fatal acute infections common to all types, on the one hand, and from subclinical persistent infections to rapidly progressive chronic liver disease with cirrhosis and even hepatocellular carcinoma, common to the blood borne types (HBV, HCV, and HDV), on the other. Chronic hepatitis is defined as hepatic necro- inflammation (detectable by biochemical or histological methods) continuing for more than 6 months. The condition may be self-limiting but usually progresses to fibrosis and subsequent architectural distortion with regenerating nodules leading to cirrhosis.

There are many diverse causes of chronic hepatitis which can be broadly categorized into viral (Chronic hepatitis B, C and D) and non-viral causes (Alcoholic hepatitis, Non-alcoholic steatohepatitis, Wilson's disease, Drugs, Auto-immune hepatitis and others) ¹⁻³. Chronic hepatitis represents a series of liver disorders of varying causes and severity in which hepatic inflammation and necrosis continue for at least 6 months. Milder forms are nonprogressive or only slowly progressive, while more severe forms may be associated with scarring and architectural reorganization, which, when advanced, lead ultimately to cirrhosis. Measurement of Glycated hemoglobin (HbA_{1c}) is used for routine evaluation and management of patients with diabetes mellitus. Concentrations of HbA_{1c} provide a means of assessing long-term glycemic status and correlate well with development of complications related to diabetes mellitus. The liver plays a major role in regulating glucose metabolism because it is the main source of endogenous glucose and a major site involved in insulin metabolism. Liver disease is often associated with an increased prevalence of impaired glucose tolerance and diabetes mellitus. The effect of HbA_{1c} on Acute and Chronic liver diseases is not well studied. The present study is to know whether acute and chronic liver diseases have same effect on HbA_{1c} or different effects on HbA_{1c} and also to know the enzyme levels (ALT, AST and ALP) in these cases.

Glycated Hemoglobin: Glycation is the non-enzymatic addition of a sugar residue to amino groups of proteins. Human adult hemoglobin (Hb) usually consists of HbA (97%), HbA₂ (2.5%) and HbF (0.5%). HbA is made up of four polypeptide chains, 2- α and 2- β chains. Chromatographic analysis of HbA identifies several minor hemoglobins namely HbA_{1a}, HbA_{1b}, HbA_{1c}, which are collectively referred to HbA₁. HbA_{1c} is formed by the condensation of glucose with N-terminal Valine residue of each β -chain of HbA to form an unstable Schiff base (Aldimine, Pre- HbA_{1c}). The Schiff base may either dissociate or undergo an Amadori rearrangement to form a stable ketoamine, HbA_{1c}, Hb A1a1 and Hb A1a2 which make up Hb A1a, have fructose-1, 6-diphosphate and glucose-6-phosphate, respectively, attached to the amino terminal of the β -chain. HbA_{1c} is the major fraction, constituting approximately 80% of HbA₁.

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AIM: To study the effect of Acute Liver Disease and Chronic Liver Disease on Glycated hemoglobin (HbA1c), Alanine transaminase (ALT), Aspartate transaminase (AST) and alkaline phosphatase (ALP) levels.

MATERIAL AND METHODS: The present study was done in Govt. General Hospital, during January 2012 to December 2013 (2 Years) in the Department of Biochemistry, Rangaraya Medical College, Kakinada, after obtaining the ethical Committee clearance. Blood samples were collected from out patients and inpatients under strict aseptic measures after obtaining the consent from the patients. It is case control study. A total number of 80 patients diagnosed and treated by Medical Department were taken for the study. Out of 80 patients, Acute liver disease patients were 40 (Acute liver disease include all Acute viral hepatitis cases in which Hepatitis B virus cases were 17 and Hepatitis C cases were 6) and Chronic liver disease patients were 40 (Chronic liver disease include Alcoholic liver disease cases 24, Hepatitis B virus cases 10 and Hepatitis C virus cases 6). Forty (40) people who are age and sex matched, apparently healthy normal subjects were also studied as controls. Chronic liver diseases group were taken as those suffering from chronic hepatitis for more than six months. The age distribution of acute liver disease patients in the present study ranged from 17-50 years (Males 30 and females 10) with a peak incidence at 22-29 years. In Chronic liver disease the age distribution ranged from 48-59 years (Males 38 and females 2) with a peak incidence at 52-55 years. Samples were analysed for HbA1c, Alanine transaminase (ALT), Aspartate transaminase (AST) and alkaline phosphatase (ALP). **Statistical analysis:** It is case control study. Analysis was done by Student's 't' test using Grphpad software.

EXCLUSION CRITERIA: Subjects who were previously diagnosed as either diabetes or anemia were excluded.

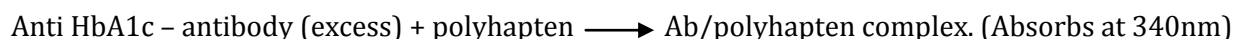
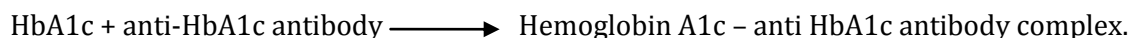
Sample collection: For HbA1c sample collection no fasting is necessary. Intravenous sample was collected. Whole blood treated with EDTA was used for analysis. Stability – 3 days at 15-25°C, 7 days at 2-8°C and 6 Months at -20°C (freeze only once). For ALT, AST and ALP unhemolysed serum

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samples were collected. ALT is stable for 3 days at room temperature, for 1 week at 2 to 8°C. AST is stable at 4°C for 7 days. ALP activity in serum is stable for 4-7 days at 2-8°C.

Measurement of HbA1c by turbidimetric inhibition immunoassay method: Measurement was done by Siemens Dimension Xpand plus Analyzer.

Principles of Procedure: Hemoglobin A1c in the sample reacts with anti HbA1c antibody to form a soluble antigen-antibody. A polyhapten reagent containing multiple HbA1c epitopes is then added to this cuvette. The polyhapten reacts with excess (free) anti-HbA1c antibodies to form an insoluble antibody-polyhapten complex. The rate of this reaction is measured turbidimetrically at 340nm and blanked at 700nm and is inversely proportional to the concentration of HbA1c in the sample.

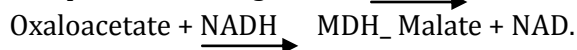


The principle for ALT estimation is: IFCC Method, Kinetic.



Absorbance is measured at 340nm wavelength.

The principle of AST estimation is: IFCC Method, Kinetic.



(AST: Aspartate aminotransferase. MDH: Malate dehydrogenase. LDH: Lactate dehydrogenase)

Absorbance is measured at 340nm wavelength.

The principle of ALP estimation is: (Adaptation by Wilkinson et al of the Bessey. Lowry et al method)



Absorbance is measured at 405nm wavelength. (Serum samples were collected for ALT, AST and ALP estimation.)

RESULTS: A total number of 80 cases, out of which 40 cases of acute liver disease and 40 cases of chronic liver disease were taken in the study. 40 people who are age and sex matched, apparently healthy normal subjects were also studied as controls. Statistical analysis was done by student's 't' test using Graphpad software. Control group were compared with acute liver disease group and chronic liver disease group. HbA1c of Acute liver disease shows no statistical significance when compared with controls. But HbA1c of Chronic liver disease shows statistical significance when compared with control ('P' value < 0.01). ALT, AST and ALP of Acute liver disease and Chronic liver

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disease when compared with control shows very high significance ('P' value < 0.001). Table 1 Shows t and p values and Table 2 shows Mean SD values of various parameters in control group, acute liver disease and Chronic liver disease. Table 3 shows normal reference range.

| Parameter | Control vs. Acute liver disease | | Control vs. Chronic liver disease | |
|-----------|---------------------------------|-----------------|-----------------------------------|-----------|
| | 't' value | 'p' value | 't' value | 'p' value |
| HbA1c | 1.86 | Not significant | 2.62 | < 0.01 |
| ALT | 21.82 | < 0.001 | 15.77 | < 0.001 |
| AST | 28.45 | < 0.001 | 22.17 | < 0.001 |
| ALP | 33.1 | < 0.001 | 33.36 | < 0.001 |

Table 1: showing 't' value and 'p' value in Control vs. Acute liver disease and Control vs. Chronic liver disease

DISCUSSION: In the present study HbA1c of Acute liver disease group when compared with control group, HbA1c mean value is decreased in acute liver disease (Table 2, Bar Diagram 1). But statistically it is not significant. Acute viral hepatitis results in serious impairment in hepatic glycogen synthesis and gluconeogenesis and frequently gives rise to fasting hypoglycaemia.⁴ HbA1c of Chronic liver disease group when compared with control group shows increased HbA1c values and statistically more significant ('P' value < 0.01) (Table 1) which may be due to endogenous insulin resistance which causes impaired glucose tolerance. Chronic liver disease has significant impact on hepatic glucose metabolism. Similar results were observed by Clara Megyesi M.D. Budapest.⁵⁻⁸

ALT, AST and ALP values of Acute liver disease and Chronic liver disease groups when compared with control group shows statistically very high significance ('P' value < 0.001) (Bar diagram 2). Liver disease is most important cause of increased transaminase activity in serum. Very high level of transaminase activity is seen in acute liver disease than Chronic liver disease. ALP increases in Hepatobiliary disease (Biliary obstruction).⁹

CONCLUSION: Acute liver disease group shows no significant increase in HbA1c when compared with control, but Chronic liver disease group shows significant increase in HbA1C when compared with control group, which may be due to endogenous insulin resistance which causes impaired glucose tolerance. Chronic liver disease has significant impact on hepatic glucose metabolism. ALT, AST and ALP values of Acute and Chronic liver diseases increased and show very high significance due to Liver disease and biliary obstruction in certain cases. Limitation of the study is with respect to the sample size and individual diseases are not studied.

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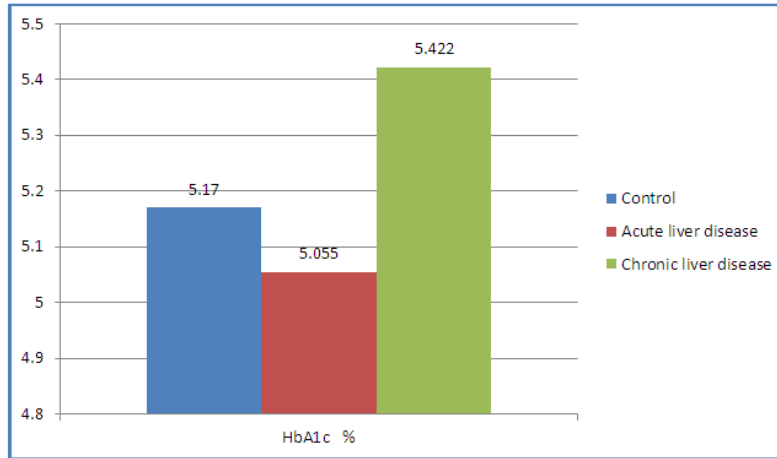
| Parameter | Control | Acute liver disease | Chronic liver disease |
|-----------|---------|---------------------|-----------------------|
| HbA1c | 5.170 | 5.055 | 5.422 |
| % | ± 0.290 | ± 0.262 | ± 0.536 |
| ALT | 17.88 | 97.13 | 46.10 |
| U/L | ± 4.11 | ± 22.59 | ± 10.54 |
| AST | 17.40 | 87.25 | 44.25 |
| U/L | ± 3.00 | ± 15.23 | ± 7.04 |
| ALP | 19.28 | 92.13 | 111.83 |
| U/L | ± 4.97 | ± 13.00 | ± 16.82 |

Table 2: Mean ± SD values of various parameters in controls, Acute liver disease and Chronic liver disease

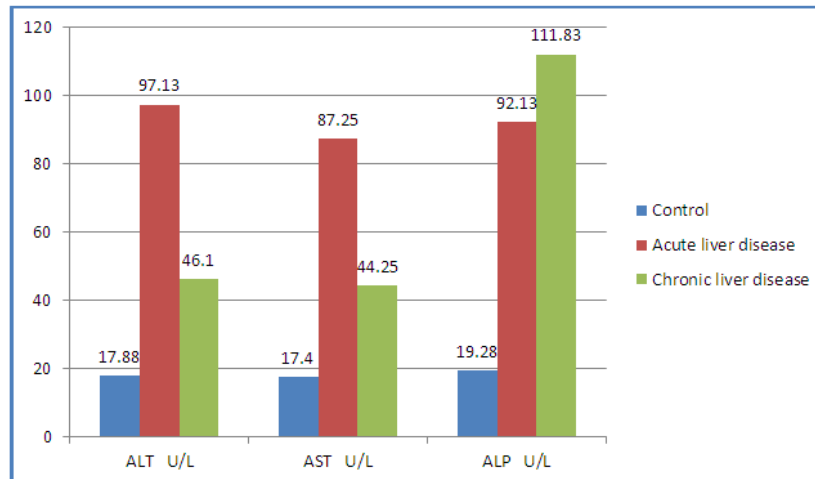
| Parameter | Method | Reference range |
|---------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| HbA _{1c} % | Turbidimetric inhibition immunoassay Siemens Dimension Xpand plus Analyzer | 4.8-6 % |
| ALT U/L | IFCC Method, Kinetic. Erba Autoanalyser. | Females: Up to 22 IU/L at 30 ^o C or 0-31 IU/L at 37 ^o C Males: Up to 29 IU/L at 30 ^o C or 0-40 IU/L at 37 ^o C. |
| AST U/L | IFCC Method, Kinetic. Erba Autoanalyser. | 8-22 IU/L at 30 ^o C, or 5-34 IU/L at 37 ^o C |
| ALP U/L | Tris / Carbonate Buffer, Kinetic. Erba Autoanalyser. | 12-90 IU/L at 30 ^o C 15-112 IU/L at 37 ^o C |

Table 3: Normal Reference range

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Bar Diagram 1



Bar Diagram 2

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