

COMPARATIVE STUDY OF LIVER FUNCTION TESTS IN DIABETES TYPE-2 PATIENTS AND NON-DIABETICS IN GUJARAT

Vishaldeep D Gohel*, Betsy Johnson**, Varsha Joshi***,

*Tutor, **2nd Year resident, *** Head of department, Department of Physiology, Shree M.P.Shah Government Medical College, Jamnagar 361008

Abstracts: Background: Diabetes mellitus is one of the major non-communicable diseases and the prevalence is rising globally. Abnormal liver function tests are not uncommon encounter in diabetes mellitus patients. **Objective:**-In this study aim was to find out the liver function test abnormalities in diabetic type-2 patients in Jamnagar, Gujarat. **Material and Method:** - this cross sectional study was conducted at the diabetic clinic in Guru Govind Singh General hospital, Jamnagar between May 2011 and May 2013, a total 200 patients were included. Parameters like serum Bilirubin (total & direct), total protein, serum albumin, alanine aminotransferase (ALT), alkaline phosphatase (ALP) used. **Result:**- 37% of diabetics type -2 patients had elevated total bilirubin value while in control group 6% had elevated value. Normal total protein, serum albumin level in both groups. Raised ALT were noted in 39 % of diabetes type -2 patients while in control group 6% had elevated value. Elevations in serum alkaline phosphatase (ALP) were found in 38 % of diabetic type – 2 patients while in control group had not much elevated value. Mean value of ALT & ALP had no correlation with gender of the diabetes patients. **Conclusion:** - abnormal liver function results are more common among diabetes patients. There were not significant changes in parameters like serum Bilirubin (total & direct), total protein, serum albumin. But elevated ALT and ALP are the markers for associated non-alcoholic fatty liver disease in diabetes patients.

Key Words: diabetes mellitus, liver function, serum Bilirubin total protein, serum albumin, alanine aminotransferase (ALT), alkaline phosphatase (ALP)

Author for correspondence: Dr. Vishaldeep D Gohel, Department of physiology, Shree M.P. Shah Government Medical College, Jamnagar 361008. e- mail: Vishaldeep.gohel47@gmail.com

Introduction:

Diabetes mellitus is one of the major non-communicable diseases and the prevalence is rising globally. Type 2 diabetes is the most common form, accounting for 90% of all cases¹. Liver has a major role in glucose homeostasis and in diabetes mellitus hepatic carbohydrate metabolism is commonly disturbed.

However, in diabetic patients, the prevalence of abnormal LFT results and their relationships to clinical findings and diabetes per se, as well as to pathologic changes in liver structure, are controversial². There exists an association between diabetes and liver injury. Liver plays a major role in the regulation of carbohydrate homeostasis. The total number of diabetes is projected to increase from 171 million in 2000 to 366 million in 2030. Diabetes is more prevalent in men than women³. Hepatocellular glycogen accumulation leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients. In hyperglycemic states, there will be intracellular glycogen accumulation in the hepatocytes due to increased glycogen synthesis, causing typical

biochemical findings of mild to moderately elevated aminotransferases, normal liver synthetic function, with or without mild elevations of alkaline phosphatase. All these biochemical disturbances and hepatomegaly are found to be reversible with good glycaemic control³

The steatosis is either micro vesicular or macro vesicular and is found to progress to fibrosis and cirrhosis. The most common clinical finding is hepatomegaly, with normal or only mildly elevated transaminases and normal bilirubin These changes are not reversible with sustained glucose control⁴

Non-alcoholic fatty liver disease (NAFLD) is the main cause of chronic liver disease associated with diabetes and obesity. Without treatment, compensated steatosis in NAFLD will eventually lead to decompensated steatosis with necroinflammation and fibrosis, i.e stage of non-alcoholic steatohepatitis (NASH). NASH is a leading cause of end-stage liver disease and also a contributor of cardiovascular disease in type 2 diabetes mellitus⁵

Definitive diagnosis of NASH requires liver biopsy. Lifestyle modification is the

gold standard in the management of NASH. Serum amino transferases such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) indicate the concentration of hepatic intracellular enzymes that have leaked into the circulation. These are the markers for hepatocellular injury and are used as primary screening of NASH⁵. Chronic mild elevations of ALT and AST are seen in type 2 diabetes patients. So aim was to find out the liver function test abnormalities in diabetic type-2 patients. So aim of this study was to find out the liver function test abnormalities in diabetic type-2 patients.

Material and Methods:

The study was conducted on 200 cases after obtaining permission from Institutional Ethics Committee This study was a hospital based cross sectional descriptive study conducted at the diabetic clinic of G.G.H. Hospital, Jamnagar between May 2011 and May 2013. Subjects were recruited according to simple random sampling method meeting the selection criteria.

Inclusion Criteria:-The patients with confirmed diabetes mellitus or newly diagnosed diabetes mellitus by WHO criteria (1999), fasting plasma venous glucose of 126 mg/dl or random or two hour post prandial plasma blood glucose of 200 mg/dl.

Exclusion Criteria:- The diabetic patients with history of alcohol intake, hepatotoxic drugs like amiodarone, anti-tuberculous drugs, history of liver diseases or clinical evidence of acute hepatitis, those who were found to have evidence of hepatitis B and C virus infection (HBsAg positive and HCV antibody positive) were excluded from this study. Not willing to participate in study. Having liver and/or biliary diseases. Pregnant females for exclusion of gestational diabetes.

Subjects were explained the purpose and protocol of the study. After informed consent, blood sample were collected to measure following liver function parameters:

- Serum Bilirubin (Total & Direct)
- Total Protein
- Serum Albumin
- Serum alanine aminotransferase (ALT)
- Serum Alkaline phosphatase (ALP)

Statistics

• Mean & SD were calculated. Unpaired student's 't' test was applied to test difference between means. Pearson Correlation co-efficient (r) calculated to test correlation between parameters. Statistical significance was accepted at P value of <0.05.

Result: • This study includes 100 diabetic subjects and 100 age and sex matched controls.

Table:1 Study variables in comparison between Diabetics and Control groups

| | Diabetics (N=100) | Control (N=100) |
|-------------------------|-------------------|-----------------|
| Age (years) | 54.29 ± 14.58 | 49.59 ±12.09 |
| Sex ratio (Male/Female) | 68/32 | 68/32 |
| Duration of DM (years) | 4.3 ±2.36 | ----- |

Table:2 : Comparison of liver function tests in diabetics and controls (values are mean ±SD)

| | Diabetics (N=100) | Controls (N=100) |
|--------------------------|-------------------|------------------|
| RBS (mg/dl) | 166.54±31.2 | 97±18.85*** |
| Total bilirubin (mg/dl) | 0.87±0.51 | 0.69±0.12 |
| Direct bilirubin (mg/dl) | 0.35±0.21 | 0.28±0.11 |
| Total protein (gm%) | 6.61±0.50 | 5.77±0.40 |
| Serum albumin (gm%) | 3.53±0.45 | 3.66±0.37 |
| Serum ALT (U/L) | 35.25 ±10.80 | 21.89±7.73*** |
| Serum ALP (U/L) | 171.89±80.88 | 160.95±52.35 |

***P<0.001

Table 2 shows significant elevated serum ALT in diabetic group as compare to control group. There is no significant difference in Serum Bilirubin, protein, albumin & ALP value in both groups.

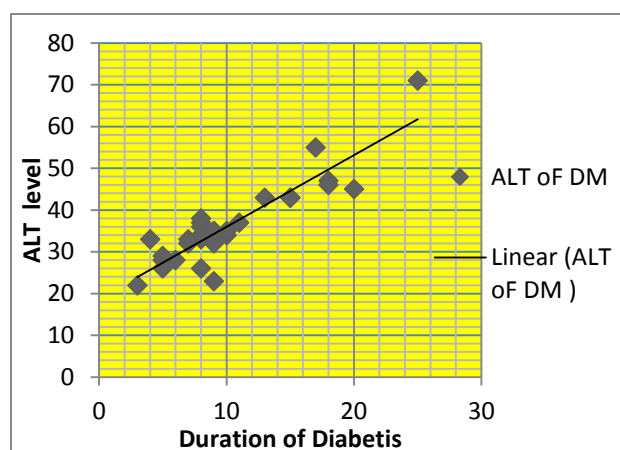
Table 3. Comparison of liver function tests in male and female diabetics (values are mean ±SD)

| | Male (N=68) | Female(N=32) |
|-------------|--------------|--------------|
| Age(years) | 54.6±14.3 | 53.7±15.83 |
| RBS (mg/dl) | 154.33±28.49 | 178.5±23.50 |
| Total | 0.94±0.62 | 0.73±0.13 |

| | | |
|---------------------------------|--------------|-------------|
| billirubin(mg/dl) | | |
| Direct billirubin(mg/dl) | 0.38±0.24 | 0.28±0.07 |
| Total protein(gm%) | 6.58±0.57 | 6.67±0.35 |
| Serum albumin(gm%) | 3.48±0.52 | 3.6±0.28 |
| Serum ALT (U/L) | 36±10.38 | 33.9±11.97 |
| Alkaline phosphatase(U/L) | 187.33±95.96 | 164.1±29.86 |

Table 3 shows there is not a significant difference in liver function test parameters in both groups.

Graph- 1: Correlation of duration of DM with Serum ALT level



Graph shows that there is positive correlation between duration of diabetes and serum ALT level.

Discussion: Type 2 diabetes patients have been reported to be associated with higher incidence of abnormal liver function tests (LFT) compared to the individuals without diabetes, elevated ALT being the most common abnormality.

Among case 37% of patient had elevated total bilirubin value while in control group only 6% had elevated value. The chi square value is 11.3206 at degree of freedom 1 the p value is 0.7564, so the test result is not highly significant, it proves that in diabetic patients the Total bilirubin value is not raised.

Similar study was conducted by Shobha Luxmi[6]. shows that values of total bilirubin concentrations were significantly lower in

comparison to the control group with p value < 0.01.

so my study is not tune with study conducted by Shobha Luxmi⁷.

Among 18 % of patient had elevated or decreased total protein value while in control group 19% had elevated value. The chi square value is 0.0332 at degree of freedom 1 the p value is 0.8555, so the test result is not significant, it proves that in diabetic patients and control group has not much difference in total protein value.

Similar study was conducted by Ayman S. Idris⁸ shows that values of total protein concentrations were significantly lower in comparison to the control group with p value of 0.001 so my study is not tune with study taken by Ayman S. Idris⁸

contrast of these two studies might occurs because of my study was conducted in Indian population with other one is conducted in Sudanese population and also the diabetic patients in my study were taken anti-diabetics regularly while there is no such thing mention in other study.

Among 17 % of patient had elevated or decreased serum albumin value while in control group 19% had elevated value. The chi square value is 0.135 at degree of freedom 1 the p value is 0.712, so the test result is not significant, it proves that in diabetic patients and control group has not much difference in serum albumin value.

Similar study was conducted by Ayman S. Idris⁸ shows that values of total protein concentrations were significantly lower in comparison to the control group with p value of 0.001.

other similar study was conducted by M Prashanth⁹ shows that there is no significant difference in serum albumin level in diabetics and non-diabetics with p-value 0.896. so the p- value of my study and study conducted by M Prashanth⁹ are very close to each other . so, my study is not tune with study is conducted by Ayman S. Idris⁸ while completely tune with study conducted by M Prashanth⁹ . Among 39 % of patient had elevated ALT while in control group 6% had elevated value. The chi square value is 19.512 at degree of freedom 1 the p value is 0.00011, so the test result is highly significant, it proves that in diabetic patients has

elevated serum ALT level in comparison with control group.

| Study | Percentage of elevated ALT level |
|-------------------|----------------------------------|
| My study | 39% |
| J.WEST [10] | 15.5% |
| Parak IM [11] | 15.3% |
| Ayman S.Idris [8] | 12% |
| Han Ni [12] | 18.5% |

J.WEST's ¹⁰ study 12.1 % of patient has elevated Serum ALT level. And p value of the J.WEST's test is also < 0.001 so it is highly significant that patient with type-2 diabetes has higher level of serum ALT level in comparison with non diabetics. So my study is completely tune with J.WEST's study.

Similar study was conducted by Paruk IM ¹¹ shows that elevations in serum alanine transaminase were found in 15.3% (n = 48) This study was conducted in South African black and Indian adult patients with type 2 diabetes mellitus attending a tertiary diabetes clinic. So my study is completely tune with Paruk IM's study.

Similar study was conducted by Ayman S. Idris ⁸.this study was conducted in International University of Africa, Sudan . This study shows that elevations in serum alanine transaminase were found in 12 % (n = 50) , p value of this study was 0.001 so it is highly significant that patient with type-2 diabetes has higher level of serum ALT level in comparison with non-diabetics. So my study is completely tune with Ayman S. Idris ⁸ study.

Similar study was conducted by han Ni ¹² this study was conducted in Singapore General Hospital, 169608, Singapore. This study shows that elevations in serum alanine transaminase were found in 18.5 % (n = 50), p value is 0.0103 so it is significant that patient with type-2 diabetes has higher level of serum ALT level in comparison with non-diabetics. So, my study is completely agreed with by han Ni ¹¹.

In comparison with other studies my study shows higher percentage of elevated serum ALT level, possible reason is that in my study patients does not control their blood glucose level

properly so there is more chance of high glucose level. High glucose level for prolong period is more prone to liver toxicity and liver injury leads to release of ALT and other enzymes in the circulation so level of liver enzymes are increased.

This study shows that elevations in serum ALP were found in 38 % in diabetes patients (n =100) , p value of this study was 0.002 so it is highly significance that patient with type-2 diabetes has higher level of serum alkaline phosphatase level in comparison with non diabetics.

Similar study was conducted by Paruk IM ¹¹. this study was conducted in Obafemi Awolowo University, Ile-Ife, Nigeria. This study shows that elevations in serum ALP were found in 23.3 % (n = 73), p value is 0.013 so it is significance that patient with type-2 diabetes has higher level of serum alkaline phosphates level in comparison with non diabetics So my study is completely tune with by Paruk IM ¹¹ .

Similar study was conducted by Shobha Luxmi ⁷ .this study was conducted at the medical outpatient department of Jinnah postgraduate medical centre, Karachi from September 2006 to March 2007. This study shows that elevations in serum alkaline phosphatase were found in 25.2% (n = 120), p value is 0.013 so it is significance that patient with type-2 diabetes has higher level of serum alkaline phosphates level in comparison with non diabetics. So my study is completely tune with by Shobha Luxmi ⁷ .

Limitation:-

In over study we take 100 diabetic type 2 patients and 100 non-diabetic. If we take a larger sample size that will be more conclusive as compare to study conducted by us.

Conclusion:

Individuals with type 2 diabetes have a higher incidence of LFT impairment than individuals who do not have diabetes. The most common alteration is elevated ALT and ALP. The duration of DM significantly correlates with ALT levels. Insulin resistance in DM type-2 affecting liver metabolism is probably altering liver function tests.

References:

1. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its

- complications: estimates and projections to the year 2010. *Diabetes Med* 1997; 14(5): 81–85.
2. Pasii. Salmela, Eero A. Sotaniemi, et al. Liver Function Tests in Diabetic Patients, *Diabetic Care* 1984,1(3): 248-254..
 3. Wild S, Roglic G, Green A, Sicree R, King H. Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004; 27(5):1047–1053.
 4. Levinthal G.N, Tavill A.S. Liver disease and diabetes mellitus. *Clin Diabetes* 1999; 17 (2): 1–20.
 5. Kenneth Cusi. Nonalcoholic fatty liver disease in type 2 diabetes mellitus. *Current Opinion in Endocrinology, Diabetes & Obesity* 2009; 16:141–149.
 6. Meybodi M A, Afkhami-Ardekani M, Rashidi M. Prevalence of Abnormal Serum Alanine Aminotransferase Levels in Type 2 Diabetic Patients in Iran. *Pakistan Journal of Biological Sciences* 2008; 11: 2274-2277.
 7. Shobha Luxmi, Rukhsana Abdul Sattar et al. Association of Non Alcoholic Fatty Liver with type 2 Diabetes Mellitus. *JLUMHS* 2008.
 8. Ayman S. Idris, Koua Faisal et al. Liver function tests in type 2 Sudanese diabetic patients, *International Journal of Nutrition and Metabolism* 2011; 3(2) : 17-21
 9. M Prashanth, HK Ganesh, MV Vimal et al. Prevalence of Nonalcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus, *JAPI* 2009 ; 57
 10. J WEST, Alan Wall, Parijat De. Prevalence of abnormal liver function tests in patients with diabetes mellitus *Endocrine Abstracts* 2007; 13:157.
 11. Paruk IM, Pirie FJ, et al. High prevalence of abnormal liver enzymes in South African patients with type 2 diabetes mellitus attending a diabetes clinic, *JEMDSA* 2011 ; 16 (1): 45-49.
 12. Han Ni*, Htoo Htoo Kyaw Soe, et al. Determinants of Abnormal Liver Function Tests in Diabetes Patients in Myanmar, *International Journal of Diabetes Research* 2012, 1(3): 36-41.

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