

RESEARCH ARTICLE

Hepatic Dysfunction in Diabetes Mellitus: Biochemical and Ultrasonological Study

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Abstract

A cross-sectional study was conducted among 100 patients of type 2 diabetes in the OPD to evaluate hepatic dysfunction. The objectives of the study are to clinically evaluate patients with type 2 DM for the presence of hepatic dysfunction and to find out liver changes both ultrasonologically and biochemically in type 2 diabetic patients. This prospective study was conducted on type 2 diabetic cases admitted as well as attending OPD in Sri Siddhartha Medical College and Hospital, Tumkur, between October, 2011 and April, 2013. The cases who were diagnosed as type 2 diabetic, irrespective of duration of the diabetes were selected randomly. The mean age of the patients was 59.32 years. Majority of type 2 DM patients belonged to 51-60 years age group. Females outnumbered males in this study. The maximum duration of DM was 20 years and minimum duration was one year. Majority of males and females had diabetes for 1-5 years. Out of 100 patients, 51% had good glycemic control (HbA1c ≤ 7) and 49% had unsatisfactory glycemic control (HbA1c > 7). About 54% of the patients had minimum 1 abnormality of the liver function tests. Majority of the diabetics were aged between 51-60 years. Liver function test abnormalities were found in 54 patients (54%) showed a direct relationship with increasing duration of diabetes since diagnosis ($p=0.007$). HbA1c value > 7 is associated with 37% of cases with abnormal LFTs ($p=0.000$). The results bear out the close relation between diabetics and liver functions. In our study, age of the patient did not seem to have definite influence on effect of diabetes on liver function tests. But, the duration of diabetes did seem to have some influence on effect of diabetes on the functions of liver. These results show that poor the glycemic control, the frequency of abnormal liver function increases.

Keywords: Hepatic dysfunction, cross-sectional study, type 2 diabetes, glycemic control, liver function test.

Introduction

Diabetes mellitus is an important and commonest of all forms of endocrine disorder. It is perhaps one of the oldest diseases affecting mankind. Today, diabetic patients are living a longer life much longer than any diabetic could imagine at the beginning of the present century. With the increase in life span of diabetes, the long term complications of diabetes are seen more often. However, the involvement of the liver in diabetes is not often focused upon. Liver plays an important role in the carbohydrate metabolism and in homeostatic regulation of blood sugar level. It stores sugar as glycogen when the needs of the tissues are satisfied, but when they are unsatisfied, liberates glucose into blood either by glycogenolysis or neo-glucogenesis from non-carbohydrate sources. Hence, the attention of research workers has long been centered on the liver in the study of diabetes mellitus. Diabetes is no longer regarded as a simple disturbance in the carbohydrate metabolism, but a complex metabolic disturbance involving carbohydrates, protein, fats and electrolytes and the liver plays important roles in the metabolism of these disorders has been studied extensively, our knowledge is still small owing to lack of precise methods of assessing many of the diverse activities of this organ.

Liver has a role in pathogenicity of type 2 diabetes mellitus and also being affected adversely by diabetes. Historically, the development of diabetes in patients with cirrhosis is well documented with overt diabetes present in up to 70% of cirrhotic subjects. However, evidence is emerging that the development of chronic liver disease and progression to cirrhosis may occur after the diagnosis of type 2 diabetes and that diabetes plays a role in the initiation and progression of liver injury (Hickman and Macdonald, 2007). The present study is aimed to evaluate type 2 diabetic patients for the presence of hepatic dysfunction.

Materials and methods

Patients: This prospective study was conducted on type 2 diabetic cases admitted in Sri Siddhartha Medical College and Hospital, Tumkur, as well as patients attending medicine OPD's of this hospital between October 2011 and April 2013. The cases who were diagnosed as type 2 diabetic, irrespective of duration of the diabetes were selected randomly.

Inclusion criteria: All type 2 diabetics-diagnosed and receiving treatments or on diet control were included in the study.

Exclusion criteria: Those patients who gave history of consuming alcohol. Patients receiving hepatotoxic drugs which may alter the liver function was carefully elicited. Those patients with certain other diseases which might affect the liver function i.e., cases with severe malnutrition, recent myocardial infarction, gross infective and inflammatory process etc. Old, debilitated serious ill patients are excluded from the study as they might have altered liver function.

Collection of data: Cross-sectional study was done in type 2 diabetic patients. Study intends to find out liver changes both ultrasonologically and biochemically in type 2 diabetes mellitus. After properly selecting the case the following study methods we applied routinely in each case.

- I. Thorough clinical assessment of the case including complications of diabetes.
- II. Routine laboratory investigations
 1. Haemogram–Hb%, TC, DC, ESR, PS, PCV, MCV, Platelet count.
 2. Bleeding time, clotting time, prothrombin time.
 3. Urine analysis–colour, reaction, specific gravity, sugar, ketone bodies, albumin and microscopic examination for cells, casts.
 4. Stool analysis–for ova, cysts, occult blood.
 5. Blood sugars–fasting blood sugars, 2 h post prandial blood sugar.
 6. Glycosylated hemoglobin (HbA1C).
 7. RFT–BUN, Serum creatinine.
 8. LFT–Using computerized autoanalyser.
 - a) Total bilirubin
 - b) Direct bilirubin
 - c) Total protein
 - d) Albumin
 - e) AST
 - f) ALT
 - g) Alkaline phosphatase

Imaging of liver: Ultrasonographic examination of abdomen was carried out at the Radiology Dept. of Sri Siddhartha Medical College and Hospital to determine the size, echogenicity of liver and the presence of fatty liver.

Statistical analysis: The data thus obtained was compiled and transferred to Statistical Package Social Services (SPSS vs 18). The categorical variables were presented as frequencies and percentages. The quantitative variables were presented as means and standard deviations. Chi-square test was used as significance test for categorical variables. A regression analysis was used. A p value of <0.05 was considered as statistically significant.

Results

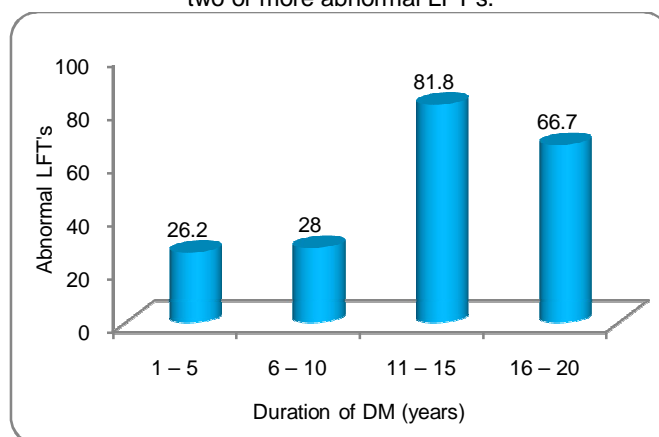
Three patients were in the age of 31-34 years, 21 patients were in the age of 45-50 years, 21 patients were in the age of 51-55 years, 17 patients were in the

age of 56-60 years, 15 patients were in the age of 61-65 years, 6 patients were in the age 66-70 years, 12 patients were in the age of 71-75 years, 3 patients were in the age of 76-80 years, 2 patients were in the age group of more than 80 years. Out of 100 patients, 61 are having diabetes for 1-5 years with 29 (59.2%) males and 32(62.7%) females, 25 are having for 6-10 years with 2(24.5%) males and 13(25.5%) females, 11 are having for 11-15 years with 6(12.2%) males and 5(9.8%) females, 3 are having for 16-20 years with 2(4.1%) males and 1(2.0%) females. Out of 100 patients, 51% had good glycemic control (HbA1c ≤7) and 49% had unsatisfactory glycemic control (HbA1c >7) (Table 1).

Table 1. Glycosylated haemoglobin levels of diabetic patients (n =100).

HbA1c	No. of cases	Percentage
≤7	51	51
>7	49	49

Fig. 1. Relation of duration of diabetes mellitus with two or more abnormal LFT's.



On examining the duration of diabetes mellitus with two or more abnormal liver function tests, 26.2% of the patients with 1-5 years duration, 28% with duration of 6-10 years, 81.8% with duration of 11-15 years and 66.7% with 16-20 years had two or more abnormal liver function tests. The distribution of diabetic patients depends upon the number of normal and abnormal LFTs and HbA_{1c} levels (Fig. 1). About 66.7% of the patients with HbA_{1c} levels of <7% had no abnormal LFT. About 24.5% of the patients with >7% had no abnormality. About 22.4%, 28.6%, 14.3% and 8.2%, 2% of the diabetics who had more than 7% HbA_{1c} had one, two, four, three and five LFT test abnormalities (Table 2). Total serum bilirubin was increased in 17 cases (17%) in this study, but not so significantly raised. A maximum value of 2 mg/dL was observed in one case. Total protein was decreased in 10 cases (10%). Lowest value of 6.2 mg/dL was observed in two cases. Albumin was decreased in 26 cases (26%) in this study. Lowest value of 2.4 mg/dL was found in one case.

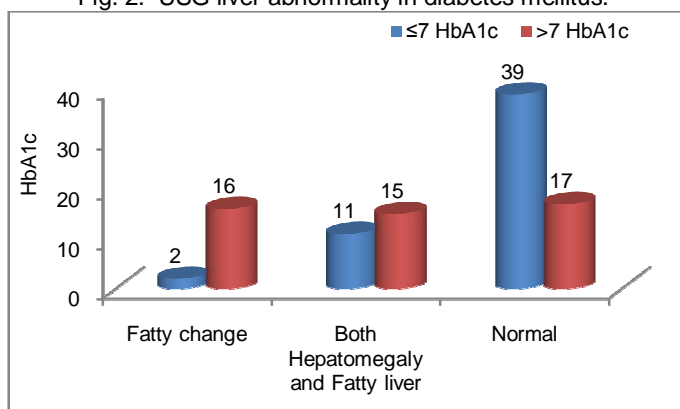
Table 2. Relation of glycemc control with abnormal LFT.

Number of abnormal LFT findings	HbA _{1c}		Total
	≤7 n (%)	>7 n (%)	
No abnormality	34 (66.7)	12 (24.5)	46 (46.0)
One	9 (17.6)	11 (22.4)	20 (20.0)
Two	7 (13.7)	14 (28.6)	21 (21.0)
Three	0	4 (8.2)	4 (4.0)
Four	0	7 (14.3)	7 (7.0)
Five	1 (2.0)	1 (2.0)	2 (2.0)
Total	51 (100)	49 (100)	100 (100)

Table 3. Relation between glycemc control and liver function tests.

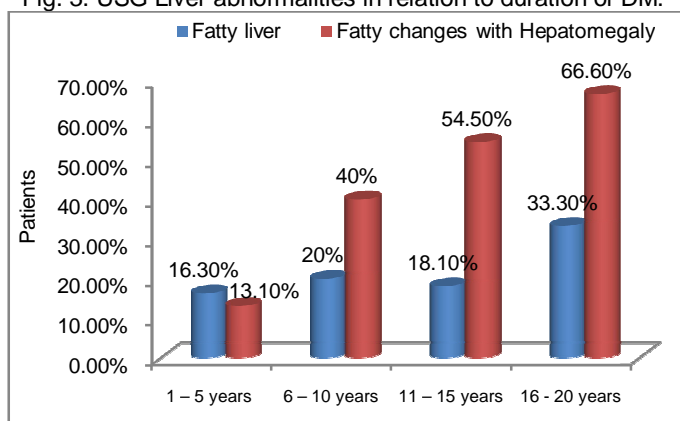
Liver function tests	HbA _{1c} levels		t value	p value, Sig
	≤7% Mean ± SD	>7% Mean ± SD		
T. Bilirubin	0.9 ± 0.2	1.0 ± 0.3	-1.783	0.078, NS
D. Bilirubin	0.1 ± 0.1	0.2 ± 0.2	-3.236	0.002, Sig
T. Protein	7.0 ± 0.4	7.0 ± 0.4	0.488	0.627, NS
Serum Albumin	3.6 ± 0.3	3.6 ± 0.4	0.737	0.463, NS
SGOT	33.8 ± 8.6	40.8 ± 12.7	-3.184	0.002, Sig
SGPT	33.5 ± 8.6	41.0 ± 13.6	-3.301	0.001, Sig
ALP	84.7 ± 24.0	96.3 ± 25.3	-2.338	0.021, Sig

Fig. 2. USG liver abnormality in diabetes mellitus.



About 26% of patients had both Hepatomegaly with Fatty changes. Fatty changes observed in 18 (18%) cases. None of the cases had cirrhotic changes. Patients with glycemc control (unsatisfactory) HbA_{1c} >7 outnumber in USG liver abnormality cases. About 26% of patients had both Hepatomegaly with Fatty changes. Fatty changes observed in 18(18%) cases. None of the cases had cirrhotic changes. Patients with glycemc control (unsatisfactory) HbA_{1c} >7 outnumber in USG liver abnormality cases (Fig. 2). The mean T Bilirubin levels were 0.9 mg/dL (±0.2) in patients with normal HbA_{1c} levels and 1.0 mg/dL (±0.3) in patients with unsatisfactory HbA_{1c} levels (Table 3). P value is significant for D Bilirubin, SGOT, SGPT and ALP. In relation to duration of DM, age group of 1-5 years showed fatty liver and fatty changes with hepatomegaly in 16.3% and 13.1%, in 6-10 years it was 20% and 40% and in 11-15 years it was 18.1% and 54.5% and in 16-20 years it was 33.3% and 66.6% respectively (Fig. 3).

Fig. 3. USG Liver abnormalities in relation to duration of DM.



Discussion

Diabetics, now lead a longer life than before and as a consequence of these, long term complications of the disease has risen. This study is an attempt towards learning and throwing some light on one of the long term complications or susceptibility of diabetics to hepatic dysfunction in the diabetic population of various ages and duration of diabetes. Liver dysfunction is a known association with diabetes. The different liver abnormalities in diabetes cover the entire spectrum from asymptomatic transaminases to cirrhosis (Harris, 2005). West *et al.* (2006) showed ALT elevation up to 9.5% (95% CI 7.1-12.3%) in type 2 DM patients. In their study, the prevalence of elevated ALT is 3-4 times higher in patients with either type 1 or type 2 diabetes than in the general population.

Serum SGOT values were found to be high in 29 cases (29%) in this study. All the cases were asymptomatic and have serum SGOT values minimally elevated. Serum SGPT was abnormally increased in 30 (30%) cases in this study. All the cases had minimal rise in SGPT values. Serum ALP-Highest value of 1781 U/L was found in one case.

Table 4. Frequency of abnormal LFT in DM in various studies.

Various studies	Incidence of one or more abnormal LFT
Idris <i>et al.</i> (2011)	22%
Paruk <i>et al.</i> (2011)	46.60%
Salmela <i>et al.</i> (1984)	57%

Frequency of abnormal LFT in DM in various studies is shown in Table 4. Salmela *et al.* (1984) studied the liver function tests of 175 diabetic patients without chronic liver disease, where 57% were found to have at least one abnormal LFT, 27% had at least two abnormal LFTs. However, these increases in liver function values were rarely more than two times of the upper limit of normal. According to a study in Sudan, where 50 diabetes patients and 30 normal control subjects were tested for liver function, the means of ALT, AST, γ GT, total protein and albumin were reported to be significantly higher among diabetes compared to the control. However, the mean values were within the normal range. In this study, 22% had at least one abnormal liver function test (Idris *et al.*, 2011). Similar finding was also present in a study by Foster *et al.* (1980), in which the means of ALT, AST, ALP, γ GT, bilirubin and albumin of 60 study subjects with diabetes were within the reference range. To eliminate the errors of hepatic dysfunction in diabetes mellitus of short duration and long duration, this study included cases of all categories of duration of diabetics, even though the largest group of patients (61%) were diabetics up to 1-5 years (Group A), there was adequate representation in Group B (duration of diabetics up to 6-10 years) of 25%, Group C (duration of diabetics up to 11-15 years) was 11%, Group D (diabetics up to 16-20 years) was 3%.

Glycylated haemoglobin (HbA1c) was estimated in all 100 diabetics to find out the glycemic control in patients with diabetics in this study, maximum number of patients (51%) were in Group I (well controlled) followed by Group II (unsatisfactorily controlled) 49% of the patients. Our results bear out the close relation between diabetics and liver functions. If the liver is altered structurally in diabetes mellitus, some functional derangement is also expected. In our study, laboratory investigation revealed abnormal liver function tests (one or more abnormal LFT) in 54% of cases and 34% of our patients showed two or more abnormal liver function tests. In this study, age of the patient did not seem to have definite influence on effect of diabetes on liver function tests. But, the duration of diabetes did seem to have some influence on effect of diabetes on the functions of liver. This study found that as the duration of diabetes increases, there was increased frequency of abnormal liver function tests, indicating clearly that more the duration of diabetes, more the effect of diabetes on functions of liver. There was 100% of the patients had abnormal liver function tests in Group D (duration of diabetes from 16-20 years), 81.8% in Group C (duration of diabetes from 11-15 years) as compared to 68% and 41.9% in

Group B (duration of diabetes up to 6-10 years) and Group A (duration of diabetes up to 1-5 years) respectively. This study next attempted to find out the relationship between glycemic control and incidence of hepatic dysfunction and found that glycemic control does seem to have a definite effect on hepatic dysfunction in diabetes. In Group I (well controlled–HbA1c ≤ 7) 17% of patients had minimum of one abnormal liver function tests and 8% of patients had two or more abnormal liver function tests. In Group II (unsatisfactory glycemic control HbA1c >7) 37% ($p=0.000$) patients had minimum of one abnormal liver function test and 26% had two or more abnormal liver function tests. These results show that poor the glycemic control, the frequency of abnormal liver function increases. This study found minimally raised SGOT and SGPT, 29% and 30% of patients respectively. About 17% of the cases had minimally raised bilirubin, all of them had total bilirubin value of less than 2 mg/dL and only one had value of 2 mg/dL. Fall in total protein in 10% and fall in albumin in 26% was noted.

Conclusion

This study included 100 type 2 diabetes mellitus patients for detection of hepatic dysfunction using biochemical and radiological methods. Prevalence of minimum 1 LFT abnormality was 54% in this study. Patients with glycemic control HbA1c value >7 are at a greater risk for developing fatty liver and LFT abnormality. So it may be concluded that early detection and optimum control of diabetes mellitus is important in minimizing the effect of diabetes on liver like other organs. A larger trail of a longer follow up period is necessary to establish the prognosis of liver diseases caused by diabetes mellitus.

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