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Research Article

Study of hepatic dysfunction in type 2 diabetes mellitus accessing healthcare services in an urban tertiary care hospital

Shilpa P. Karande*, Santosh G. Gosavi, Chinmayee P. Mishra

Department of General Medicine, T. N. Medical College and B.Y.L. Nair Ch. Hospital, Mumbai, Maharashtra, India

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***Correspondence:**
Dr. Shilpa P. Karande,
E-mail: drshilpapvk@rediffmail.com

ABSTRACT

Background: Diabetes mellitus (DM) is an extensively researched and studied subject mainly because of two factors: its, often silent spread among the community and the wide range of complications associated with it. One of them being hepatic dysfunction, the spectrum of which ranges from clinically asymptomatic with steatosis to NASH, NAFLD, cirrhosis and rarely, hepatocellular carcinoma.
Methods: This cross-sectional study was carried out in 50 patients from the general medicine OPD of a tertiary care hospital, who were selected based on certain inclusion and exclusion criteria. After clinical evaluation, routine haematological and radiological investigations in type 2 diabetic patients, mainly liver function tests, CBC, sonography of the abdomen, ECG, urine analysis, anthropometric measurements, etc were noted. Data was analyzed by using statistical package of social sciences (SPSS) version-17.0.
Results: The duration of diabetes was compared with the count of USG abdomen which came positive for fatty liver. Approximately 10 (20%) patients of type 2 DM, had symptoms of dull aching pain and 7 (14%) patients had hepatomegaly on palpation, which is clinically significant. 28% of the total study group was detected having fatty liver. Prevalence studies on this study group shows that 24.14% of the patients having diabetes less than 5 years, 40% of the patients having diabetes for more than 10 years and 31.25% of patients in the duration range of 6-10 years show evidence of fatty liver on ultrasound of abdomen.
Conclusions: Increased BMI, deranged blood sugar levels, early nephropathy and presence of retinopathy had significant clinical correlation with hepatic involvement in this study. There is a positive prevalence of liver dysfunction as detected on sonography of the abdomen, in patients with type 2 DM. A significant correlation was obtained between fasting blood sugar and BMI. This signifies that glycemic control management plays an important role in preventing complications of diabetes like central obesity and hepatic involvement.

Keywords: Hepatic dysfunction, Liver dysfunction, Type 2 diabetes mellitus, NASH

INTRODUCTION

Diabetes mellitus is one of the chronic lifestyle endocrine disorders that has been researched extensively and in various tangents, as this 'silent killer' is known to have numerous microangiopathic and macroangiopathic complications ranging from retinal, renal and liver dysfunction, cardiovascular disease, peripheral neuropathy and poorly controlled glycemic index leading to obesity and metabolic syndrome.[1]

Diabetes mellitus can alter hepatic morphology and physiology and can itself be precipitated by hepatic diseases.[2] The most common clinical presentation is hepatomegaly, and most patients have normal or only mildly abnormal transaminases and normal bilirubin. Since hepatic involvement in a type 2 diabetic patient can

range anywhere between clinically asymptomatic with steatosis to NAFLD, NASH, cirrhosis or rarely hepatocellular carcinoma. Cirrhosis was the fourth leading cause of death and accounted for 4.4% of diabetes-related deaths.[1,4] Thus, it is important to have necessary biological markers and investigations for the early detection and diagnosis of liver dysfunction in this condition.[1] This pilot study therefore, is a step towards recognising and understanding which tool can be used as a feasible marker for diagnosis of hepatic involvement in T2DM. Liver biopsy is the gold standard diagnostic test but not acceptable as a screening test, as it is an invasive procedure. It is reserved for situations of conflicting diagnosis.[3]

Liver ultrasonography (USG), although not sensitive enough to differentiate simple steatosis from more advanced hepatic involvement like NASH, is widely used as it is a feasible tool and non-invasive, hence compliance of the patients is much better as compared to liver biopsy. It is also affordable for most of the patients. Biochemical markers like AST/ALT, alkaline phosphatase, total bilirubin have been used in the study as a probable tool of detection of hepatic involvement in type 2 DM. In a study by Kalra S, prevalence of NAFLD was found to be approximately 9-32% in the general Indian population, and a higher incidence was found in obese and diabetic patients.[4]

Hence this present study was aimed to review the extent of hepatic involvement in patients with type 2 diabetes mellitus, to assess the association of hepatic dysfunction with the duration of diabetes and to assess its association with metabolic syndrome. The prevalence of hepatic dysfunction in subjects in accordance with duration of diabetes (less than 5 years, 5-10 years, more than 10 years). Furthermore, early detection and treatment will reduce the healthcare and economic burden on the individual, community and the nation.

METHODS

This cross-sectional study was carried out over a period of 3 months from July to September 2012 in 50 patients who fulfilled the inclusion and exclusion criteria and attending general medicine OPD during study period. Study was carried out with appropriate patient consent and the institutional ethics committee approval.

Inclusion criteria

Type-2 diabetic adult of either sex or age >25 years and asymptomatic for liver disease.

Exclusion criteria

All patients with type-1 diabetes mellitus, past/present history of chronic alcohol consumption, current history of Anti-Koch's therapy, past history of hepatitis or other hepatobiliary disease, history of consumption of any other drugs except oral hypoglycemic agents and anti-hypertensives and history of congestive cardiac failure, renal failure are excluded.

Methodology of the study was carried after a detailed history of all the patients in the study group, any present clinical symptoms especially dull aching pain in right hypochondriac region was noted. In general examination BMI, waist, hip ratio, acanthosis nigricans were noted. In systemic examination, emphasis was given to presence of hepatomegaly, if any. Patients were grouped according to their duration of diabetes as group 1 (=<5 years), group 2 (6-10 years) and group 3 (more than 10 years). Biochemical parameters- Hb, CBC, liver function test (AST/ALT/total bilirubin), fasting blood sugar & postprandial blood sugar, s. cholesterol, s. triglycerides, urine – routine and microscopy especially for presence of albuminuria as a marker of early nephropathy, ECG, fundoscopy for evidence of retinopathy and USG abdomen for assessment of extent of fatty liver or cirrhosis. Data was analyzed by using statistical package of social sciences (SPSS) version-17.0. Descriptive results were expressed as frequency and percentage. Statistical significance was set at $p<0.05$. Correlation coefficient was used to test for significant relationships between categorical variables.

RESULTS

A total of 50 patients (21 males and 29 females) consented for the participation with a mean fasting blood sugar-193.34 mg/dl and mean post-prandial blood sugar-277.66 mg/dl. 10 patients had symptoms of dull aching pain and 7 (14%) patients had hepatomegaly on palpation, which is clinically significant. Using USG abdomen (Table 1), 14 (28%) of the study group was detected having fatty liver. 24.14% of the patients having diabetes less than 5 years, 31.25% of patients in the duration range of 6-10 years and 40% of the patients having diabetes for more than 10 years have fatty liver. Statistical correlation of liver enzymes (AST, ALT, Sr. bilirubin) did not yield definite results. The p value was >0.05 for correlation of deranged liver enzymes with duration of diabetes for all three liver enzymes tested (AST, ALT, Sr. biliribun) (Figure 1-3). A positive correlation has been noted in association of duration of DM with presence of DMR, with 17.24% of the patients having DM <=5 years have DMR, 12.5% of patients having DM from 6-10 years and 60% in the third group of duration more than ten years have evidence of retinopathy (Table 2). The correlation between the presence of fatty liver with evidence of DMR in the study group shows 64.29% of patients who have fatty liver are also affected with DMR whereas, 16.66% of patients who do not show presence of fatty liver in the USG have evidence of DMR, (Table 3). 50% of the patients with presence of fatty liver had albuminuria. 19.44% of the patients who had normal USG also showed albuminuria, which may have been due to long standing diabetes and/or presence of nephropathy singly (Table 4). An

association has been seen between the diabetic retinopathy and diabetic nephropathy with hepatic involvement.

Table 1: Presence of fatty liver with duration of type 2 DM.

Count of USG abdomen (R)	Duration of DM (C)			
	Less than or equal 5 years	6 to 10 year	More than 10 years	Total
Fatty liver	7	5	2	14
Normal	22	11	3	36
Total	**29**	**16**	**5**	**50**

Table 2: Distribution of DMR with duration of type 2 DM.

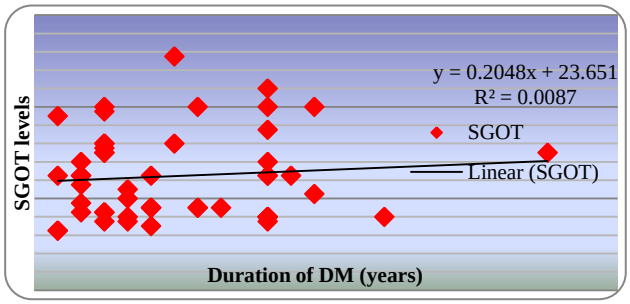
Count of fundoscopy (R)	Duration of DM (C)			Total
	Less than or equal 5 years	6 to 10 years	More than 10 years	
DMR	5	2	3	10
Normal	24	14	2	40
Total	29	16	5	50

Table 3: Presence of fatty liver on USG with fundoscopy for DMR.

Count of USG abdomen (R)	Count of fundoscopy (C)		Total
	DMR	Normal	
Fatty liver	9	5	14
Normal	6	30	36
Total	15	35	50

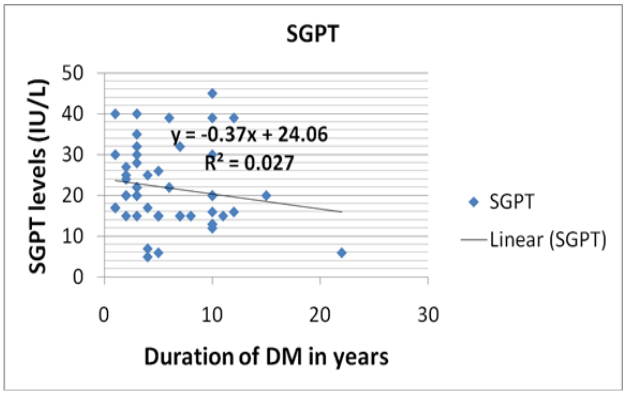
Table 4: Presence of fatty liver via urine albumin levels.

Count of USG abdomen (R)	Count of urine routine (C)		Total
	Albuminuria	Normal	
Fatty liver	7	7	14
Normal	7	29	36
Total	14	36	50



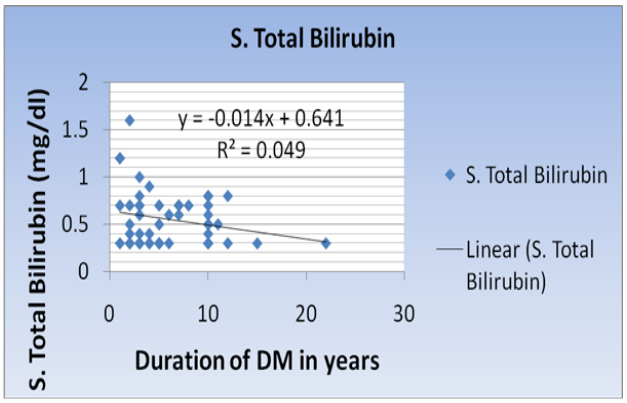
Correlation coefficient (r) = 0.09340, 95% confidence interval 0.1899 to 0.3624; P value is 0.5188, not significant.

Figure 1: Correlation between duration of DM and level of liver enzymes (AST).



Correlation coefficient (r) = -0.1642, 95% confidence interval: -0.4233 to 0.1197; P value is 0.2545, not significant.

Figure 2: Correlation between duration of DM and level of liver enzymes (ALT).



Correlation coefficient (r) = -0.2233, 95%; Confidence interval: -0.4724 to 0.05875; P value is 0.1190, not significant.

Figure 3: Correlating duration of DM with levels of serum bilirubin.

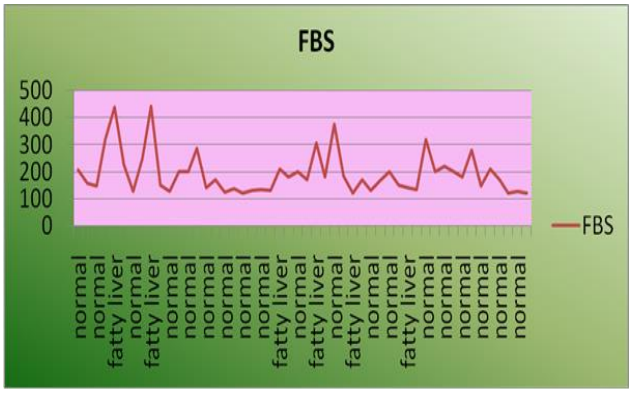
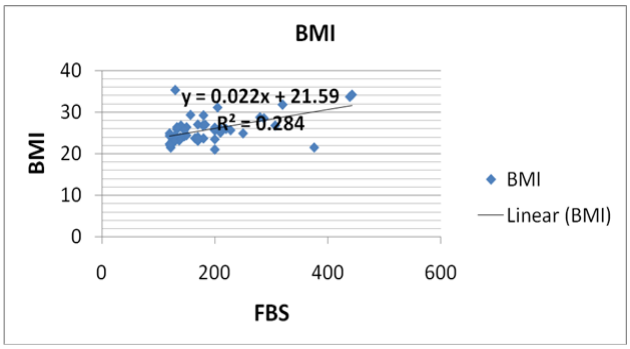


Figure 4: Correlation of P/O fatty liver with deranged blood sugars (FBS).

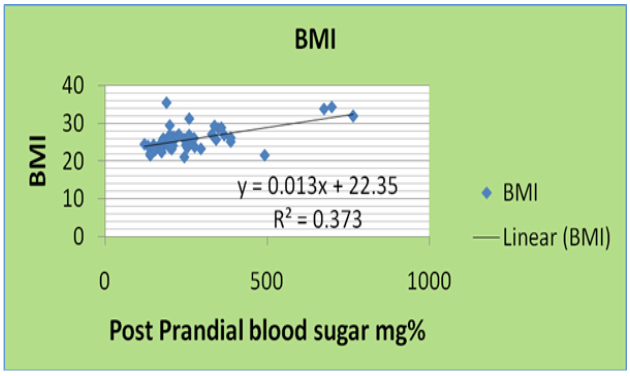
Figure 4 showed the correlation between presence of fatty liver and levels of fasting blood sugar (FBS). There is a positive correlation demonstrated by spikes in the level of FBS in cases with fatty liver. There is a positive correlation between BMI and deranged fasting and post-prandial blood sugars with p value <0.0001 in both cases

thus being extremely significant. An association of BMI derangement with hepatic involvement was seen. This is demonstrated by (Figure 5 and 6). The correlation of FBS with waist: hip ratio was found to be not significant as the p value was 0.2768 (Figure 7). 9 (64%) of patients with hepatic involvement had obesity, 7 (50%) had hypertension, 12 (85%) had dyslipidaemia which are the markers of metabolic syndrome.



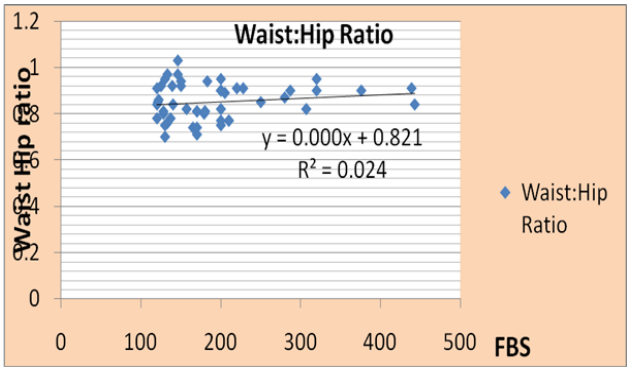
Correlation coefficient (r) = 0.5330; 95% Confidence interval: 0.2989 to 0.7066; P value is <0.0001, highly significant.

Figure 5: Correlation of BMI with levels of FBS.



Correlation coefficient (r) = 0.6112, 95% confidence interval: 0.4011 to 0.7603, P value is <0.0001, highly significant.

Figure 6: Correlation of BMI with levels of PPBS.



Correlation coefficient (r) = 0.1568, 95% Confidence interval: -0.1272 to 0.4170; P value is 0.2768, not significant.

Figure 7: Correlation between FBS and waist:hip ratio.

DISCUSSION

The duration of diabetes was compared with the count of USG abdomen which came positive for fatty liver. The results when analysed showed that there is a positive correlation of hepatic dysfunction with diabetes mellitus.[2,5] There seems to occur a higher proportion of fatty liver in those who have had diabetes for a period of more than ten years, but this should be corroborated after extensive research with a larger sample size. Most of the diabetic patients are asymptomatic, but few may have symptoms of dull aching pain in right hypochondriac region as early presentation of fatty liver. It can be demonstrated clinically by palpation for hepatomegaly. From prevalence studies with data collected using USG abdomen, 28% of the total study group was detected having fatty liver, 24.14% of the patients having diabetes less than 5 years, 31.25% of patients in the duration range of 6-10 years and 40% of the patients having diabetes for more than 10 years have fatty liver.

Correlation of LFT results (AST, ALT, s. total bilirubin) with duration of diabetes did not have much significance and the values were not deranged to a significant level even with patients having diabetes for more than ten years. Hence, these biochemical markers are not sufficient for detection of hepatic involvement in T2DM. A disadvantage of a small sample size and accountability for possible scope for laboratory error has to be taken into consideration in this study. 64.29% of patients who have fatty liver are also affected with DMR. 16.66% of patients who do not show presence of fatty liver in the USG have evidence of DMR. Also there is a positive correlation between the duration of diabetes and evidence of DMR. 17.24% of the patients in the first group (=<5 years) have DMR, 12.5% in the second group (6-10 years) and 60% in the third group of duration more than ten years have evidence of DMR. The number of studies showing this correlation are very few and scattered, hence this is an important correlation that will help the physician detect and treat early any complications like above that may arise. 50% of the patients with presence of fatty liver had albuminuria. 19.44% of the patients who had normal USG also showed albuminuria, which may be due to long standing diabetes and presence of nephropathy singly. It is observed that microangiopathic complications are associated with hepatic dysfunction in diabetics. All these results should be corroborated with studies on a larger scale as the data collected was insufficient to make a near accurate prediction. Complete LFT should be done as studies show that the values are deranged for advanced cases. Increase in GGT may be among the earliest biochemical markers, but corroboration of the same was not possible in this study.[2] Hyperbilirubinemia, prolongation of the prothrombin time and hypoalbuminemia are infrequent, although AST/ALT ratio of <1 is seen.[3,6] Liver biopsy is the gold standard for diagnosing NAFLD along with clinico-pathological correlation.[7,8] But it cannot be conducted in the Indian set-up frequently in small scale studies.

Appropriate ethics approval is required and the adequate manpower and compliance and need of the patient have to be taken into consideration. 9 (64%) of patients with hepatic involvement had obesity. In particular central obesity has been described as one of the strongest risk factors for NAFLD and fibrosis, with NASH being prevalent in 18.5% of the obese patients. 7 (50%) had hypertension, 12 (85%) had dyslipidaemia which are the markers of metabolic syndrome.[9-11]

Limitations of the study was it has been conducted on a small scale and hence all the results before being extrapolated to the population have to be conducted on a larger scale to get a greater 95% confidence interval and a more accurate mean, median, mode and standard deviation. All tests could not be conducted like HbA1c, which will change the final result accordingly.

CONCLUSION

Prevalence studies for hepatic dysfunction in type 2 DM showed a significant presence of liver involvement in the study group especially in patients with diabetes for more than 5 years of duration. Positive clinical, along with findings of sonography of abdomen, yields satisfactory results for a physician to detect and treat hepatic dysfunction in type 2 DM at an early stage. Correlation studies with liver enzymes should be carried out in larger sample sizes. A significant correlation was obtained between deranged Fasting blood sugar and BMI. There was also a significant correlation between PPBS and BMI. This signifies that glycemic control management plays an important role in preventing complications of diabetes like metabolic syndrome, central obesity and hepatic involvement. Studies have to be conducted on a large scale for extrapolation of results. Gradual weight loss and good control of blood glucose levels is recommended for patients with steatohepatitis.

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Ethical approval: The study was approved by the institutional ethics committee

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