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Original Research Article

A study on the hepatic profile of type 2 diabetic patients at a tertiary care hospital

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Abstract

Background: The prevalence of diabetes mellitus is increasing world over and is expected to affect 57 million adults in India by 2025. Apart from kidney, eye, heart and blood vessels, liver is also indirectly related with diabetes mellitus. Virtually the entire spectrum of liver disease is seen in patients with type 2 diabetes. This includes abnormal liver enzymes, non-alcoholic fatty liver disease (NAFLD), cirrhosis and acute liver failure. There are not enough studies from rural population done on the hepatic status of diabetic patients in our country. Hence this study aims to describe the hepatic profile of type 2 diabetic patients.
Materials & Methods: This is a prospective observational study where patients of diabetes mellitus with NAFLD diagnosed by USG were recruited. History and physical examination were recorded. Laboratory investigations included fasting and 2-hour post-prandial blood glucose, blood urea, serum creatinine, liver function tests, lipid profile, glycated hemoglobin were done. NAFLD was diagnosed on the basis of ultrasound assessment of the liver.
Results: We studied 200 NAFLD patients in type 2 DM, Most of the study subjects were asymptomatic and hepatomegaly was major physical sign observed we found that poor control of diabetes (p value: 0.0001) and duration of diabetes has adverse effect on NAFLD. Severity of NAFLD increases with poor control of diabetes. Obesity is a major risk factor for development of NAFLD. Waist/Hip ratio and BMI has an adverse effect on NAFLD. Dyslipidemia (75-80%) increases the incidence and severity of NAFLD. We found elevation of transaminase (57%) in our study. Metabolic syndrome (97%) is commonly associated with NAFLD.
Conclusion: Most patients were asymptomatic, Deranged transaminase and USG helps in early diagnosis of NAFLD. Obesity and dyslipidemia are major risk factors for development and progression of NAFLD. Poor glycemic control had increased incidence of NAFLD when compared to those with good glycemic control. Patients who were previously labelled as cryptogenic cirrhosis of liver are now increasingly diagnosed as having underlying NAFLD.

Keywords: Hepatic profile, type 2 diabetic patients, NAFLD

Introduction

Fatty liver disease is a condition in which there is diffuse accumulation of neutral fat in the

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form of triglycerides in hepatocytes, and is an important clinical and pathological finding. Etiologically, this arises from alcohol consumption (alcoholic fatty liver disease) or from non-alcoholic causes (non-alcoholic fatty liver disease/NAFLD).

Based on aetiology, NAFLD is classified into two types: primary and secondary. In primary NAFLD, exact aetiology remains unclear, though many studies found there is a strong association with the metabolic syndrome or any of its components, suggesting Insulin Resistance (IR) could be key factor in its aetiology [1].
Secondary NAFLD is strongly associated with possible underlying aetiological agents that include toxins, certain medications and an array of clinical conditions. Imaging techniques namely ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) will demonstrate alterations in liver architecture suggestive of increased fat in the liver. This is characteristically seen as hyperechogenicity of liver, usually called as "bright liver" on ultrasound [2].
Alcoholic fatty liver disease arises from chronic consumption of alcohol, especially in doses > 30g/day in males and 20g/day in females for long period, but can occur at lower doses. Alcohol decreases free fatty acid (FFA) beta oxidation in hepatocytes leading to triglyceride accumulation and hepatic steatosis (NASH), which can then progress to chronic hepatitis and ultimately hepatic fibrosis or cirrhosis.[3] Fatty liver disease is an important entity in view of its potential to progress to NASH then leading to cirrhosis of liver.
Recent data increasingly support a complex interplay between the metabolic condition diabetes mellitus and the pathologically defined non-alcoholic fatty liver disease (NAFLD). NAFLD predicts the development of type 2 diabetes and vice versa, and each condition may serve as a progression factor for the other. Although the association of diabetes and NAFLD is likely to be partly the result of a "common soil," it is also probable that diabetes interacts with NAFLD through specific pathogenic mechanisms. In particular, through interrelated metabolic pathways currently only partly understood [4].

Methodology

This is a prospective observational study where patients of type 2 diabetes mellitus with NAFLD diagnosed by USG were recruited. History and physical examination were recorded as per proforma. Laboratory investigations included fasting and 2-hour post-prandial blood glucose, glycated haemoglobin, blood urea, serum creatinine, liver function tests, lipid profile, were done. NAFLD was diagnosed on the basis of ultrasound assessment of the liver.
Overweight was defined as BMI between 23-27.99 Kg/mt2. Obesity as BMI >=28 kg/mt2 as per Asian standard criteria. Patients were considered centrally obese if the waist circumference was greater than >80cm in females and >90 cm in males. Patients with one of the criteria: LDL-C >= 100mg/dl, total cholesterol > 200mg/dl, TAG >=150mg/dl or HDL-C <40mg/dl in males and <50 mg/dl in females were considered to have dyslipedemia.
All patients underwent abdominal ultrasonography by the radiologist for evidence of fatty liver disease. Based on USG findings (diffuse increase in echogenisity as compare to that of spleen or renal cortex).

Ultrasonographic characteristics of fatty liver

Sonography of fatty infiltration may be varied depending on whether it is diffuse or focal. Diffuse steatosis may be mild where minimal (Grade1) diffuse increase in hepatic echopattern is seen with normal visualisation of the portal vein radicals and diaphragm & Liver echogenicity is same as compared with right kidney. Moderate (Grade 2) steatosis is seen as moderate diffuse increase in hepatic echogenicity and slightly impaired visualisation of

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intrahepatic vessels and diaphragm & Liver echogenicity is slightly increased compared with right kidney. Severe (Grade 3) steatosis appears as marked increase in echogenicity of liver compared to kidney with poor or non-visualisation of hepatic vessels and diaphragm.

Inclusion criteria

Patients of Type 2 Diabetes Mellitus with NAFLD diagnosed by Ultrasonography, belonging to both sexes and with age of more than 35 years attending department of General medicine were included in the study.

Exclusion Criteria

- Patients with history of alcohol intake more than 30 gm/day in males and more than 20 gm/day in females.
- Persons with previous history of primary liver disorders, jaundice, ascites and signs of liver cell failure are excluded.
- Patients with history of intake of drugs like Anti tubercular drug which includes Isoniazid, Pyrazinamide and Rifampicin etc. Methotrexate, Amiodarone, Glucocorticoids, Synthetic Estrogens, Nucleoside Analogues (ddI, AZI) are excluded.
- Secondary Diabetes, GDM, Type1 diabetics.
- Metabolic liver disorders.
- Persons with history of Chronic Renal Failure and severe Ischemic Heart Disease are excluded from the study.

Study design

- Two Hundred patients of NAFLD in type 2 diabetic patients newly diagnosed or on follow-up were included in this study.
- It's a cross sectional study and random selection was done.

Results

Ultra sonogram of the liver shows increased Liver echogenicity. Portal venule walls are less prominent than normal. Echogenicity of liver Parenchyma compared with Diaphragm, spleen and right Kidney. Increase in echogenicity of liver compared to diaphragm, spleen and right Kidney suggest different grades of NAFLD.

Table 1: Grades of NAFLD diagnosed by USG

Grades of NAFLD	Total	%
Grade 01	150	75
Grade 02	32	16
Grade 03	18	9
Total	200	100

As all the diabetic subjects were screened for NAFLD as per standard ultrasonographic criteria(American criteria) and most of them were asymptomatic, Grade 1 fatty liver was seen in 75% cases, suggesting early infiltration of liver with fat, the most common in our study population (n=150) grade 2 & Grade 3 NAFLD was seen in less number of cases. Grade 2 fatty liver accounted for 16% (n=32) and Grade 3 fatty liver 9% (n=18).

Table 2: Relationship of variables (Mean ± SD) to grading of NAFLD in study population

Variables		Grade 1	Grade 2	Grade 3	P value
Age(yr)		53.41±12.78	57.47±14.87	60.83±10.96	0.033
Systolic blood pressure (mm Hg)		145.53±27.30	151.56± 26.34	143.94 ±27.13	0.484
Diastolic blood pressure (mm Hg)		86.75±13.19	89.25 ±9.73	86.55±9.30	0.574
Body mass index (kg/m2)		26.47±2.43	26.72±2.65	29.23±3.53	0.0001
Waist circumference (cm)		91.25 ± 5.82	93.91 ±3.47	96.94 ±3.68	0.0001
Fasting blood sugar (mg/dl)		149.33±25.96	153.37±28.20	178.67±19.15	0.0001
Post prandial blood sugar (mg/dl)		264.31±57.47	280.81±53.90	322.00±78.80	0.0001
HbA1C level		7.53±0.76	8.05±1.09	9.31 ±1.19	0.0001
Duration of Type 2 DM		6.19 ±3.93	14.71 ±5.50	22.67 ±7.08	0.0001
Total cholesterol (mg/dl)		196.82±46.41	227.94±39.38	267.05±62.87	0.0001
Serum TG(mg/dl)		154.54±43.25	177.97±35.51	187.61±52.09	0.0001
serum LDL (mg/dl)		107.65±30.17	125.87 ±23.63	120.83±13.72	0.002
HDL-C (mg/dl)	Male	36.57±5.68	35.54 ± 3.68	33.27±3.58	0.0149
	Female	37.68±5.68	34.95 ± 3.68	33.28±3.58	0.015
SGOT(U/l)		63.27 ±27.50	77.87 ±28.08	92.78±27.41	0.0001
SGPT(U/l)		77.27 ± 35.55	91.84 ± 27.17	111.22±46.25	0.0001
SGOT/SGPT		0.86 ±0.79	0.88±0.25	0.82±0.20	0.958
ALP (U/l)		135.54±51.98	161.53± 65.50	169.67±42.47	0.004

There was significant association between mean age of the subjects and grades of the NAFLD with a p value of 0.033. As mean age increases, fatty deposition increases as evidenced by higher grades of NAFLD, suggesting advanced age has adverse effect on NAFLD.

There was no statistically significant association of gender (p value: P value: 0.375) with grades of NAFLD, seen both in males and females.

Hypertension had no effect on severity of NAFLD in this study.

In our study there was strong statistical significance found between grades of NAFLD and obesity. Increasing BMI. 93.5% (n=187) of study patients with NAFLD had a BMI that was above normal. Only 6.5% (n=13) had a normal BMI. As the BMI Increased, there was worsening of NAFLD, in different grades. This was statistically significant with a p value of 0.002, making obesity as an important risk factor.

Similarly, Waist circumference & W/H ratio also had an impact on grading of NAFLD. With worsening of these parameters, there was worsening of NAFLD also. A statistically significant relation was found with the incidence of NAFLD and waist hip ratio, waist circumference with a p-value of <0.0001 and also there was statistical significance found with grades of NAFLD and waist circumference & waist/hip ratio.

In our study we found that values of FBS, PPBS and HbA1c correlated significantly with the grades of NAFLD, with p-value being, <0.0001, in all grades. This suggest that with poor glycemic control the risk of developing NAFLD proportionately increases and severity also.

There was significant difference found in the grades of NAFLD with duration of DM, more the duration and higher the grades of NAFLD (p-value 0.0001).

Analysis of the lipid profiles showed hyper cholesterolemia, hyper-triglyceridemia, increased LDL-C were significantly associated (p value <0.0001,0.0001, 0.002 respectively) with grades of NAFLD, and decreased HDL-C both in male (p value : 0.0149) & female (p value:0.015) had significantly associated with grades of NAFLD.

We found significant association of NAFLD with deranged liver function tests, of which some components were found to be markedly elevated. There was significant difference observed in values of liver function test like SGOT, SGPT and ALP (p value: 0.0001, 0.0001,0.004 respectively) in patients with worsening in different grades of NAFLD.

In our study, no association was found between hypertension (p value: SBP -0.484 DBP-0.574) and grades of NAFLD. Incidence of Hypertension in our study is 54.5%.

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Incidence of metabolic syndrome in our study was very high its 97% as most of the NAFLD patients were obese diabetics. All Grade 2 and Grade 3 NAFLD patients had metabolic syndrome in our study.

Table 3: Relationship of Liver enzymes in study population

Enzymes	Number of patients	%	Mean
SGOT (IU/L)			68.26 ±29.01
10-35 (normal)	34	16	
36-70	53	26.5	
>70	113	56.5	
SGPT (IU/L)			82.65 ± 36.79
3-45 (normal)	39	19.5	
46-90	47	23.5	
>90	114	57	
ALP (IU/L)			144.77 ± 54.84
20-128	88	44	
129-256	105	52.5	
>256	7	3.5	

Raise in the level of SGOT & SGPT of more than two times the normal value is seen in 56.5% & 57% cases of NAFLD respectively, indicating damage to liver cell due to excessive deposition of fatty acids in the hepatocytes.
Elevated liver enzymes due to increased fat deposition fat in liver leading to deranged hepatic function was seen in majority of study subjects. But the elevation of enzymes was not significant, when it is elevated considerably, they would have developed steatohepatitis.
Even though the mean ALP values were slightly increased in the present series. Only 3.5% cases of NAFLD had abnormal (More than two fold elevation) ALP, most of the other cases had normal ALP levels, indicating that there was no obstruction to bile flow in these cases.

Discussion

This study was designed to determine the clinical profile of NAFLD diagnosed by ultrasonography in 200 subjects with type 2 diabetics. U/S is a validated surrogate tool for screening for NAFLD in the absence of liver biopsy.
Incidence of NAFLD is increasing rapidly, as is its risk factor like obesity, diabetes mellitus, hypertension, dyslipedemia, which are components of metabolic syndrome, are also increasing. Of the five components of the metabolic syndrome, diabetes is the risk factor most frequently associated with NAFLD. This study further documented the prevalence of the other components of the metabolic syndrome, namely, obesity, elevated blood pressure, elevated triglyceride and low HDL-cholesterol and we sought to determine if there was significant association of these factors to NAFLD in the study subjects.
Derangements of liver function tests and hepatic spans were also analysed. Research is still being carried out to know the exact mechanism occurring in the development of NAFLD so appropriate therapies can be developed to either prevent the development of NAFLD or halt its progression to cirrhosis. Currently only weight loss through dietary measures and exercise are the only definitive treatment available which can reduce the amount of steatosis and prevent its progression into fibrosis. But this measure is not effective once fibrosis is completely established. Other measures like insulin sensitizers, antioxidants, lipid lowering agents are not fully effective. Various pharmacological measures is under investigation.
In the present study we found that values of FBS, PPBS and HbA1c correlated significantly with the grades of NAFLD, with significant p-values this suggests that with poor glycemic

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control, the risk of developing NAFLD proportionately increases. These findings were also

observed in other studies like, Giorgio Bedogni *et al*. [5] (p-value 0.007) and also in Giovanni *et al*. [6] (p-value <0.0001). but AK Agharwal *et al*. [7] (p-value 0.178)did not find any correlation of Diabetic status (poor control of diabetes) with incidence of NAFLD. They compared NAFLD with Non NAFLD, In that there was no statistical correlation between occurrence of NAFLD with diabetic control. But in our study we are comparing between poor controls of diabetes with different grades of NAFLD.

Elevation of Liver enzymes raise in SGOT, SGPT were seen in NAFLD cases, indicating deranged Liver function. We had minimal raise in Liver enzyme levels in Majority of cases of NAFLD. This finding was comparable to similar liver function derangements from other studies described by Bacon *et al*., [8] Reid *et al*. [9] and Cortez-Pinto *et al*. [10] There was significant difference observed in values of liver function test like SGOT, SGPT and ALP The enzyme elevation directly proportional to the extent of Liver involvement. In study by AK Agharwal *et al*., [7] Giorgio Bedogni *et al*., [5] Giovanni *et al*. [6] statistically significant correlation was found between SGOT, SGPT, ALP values and occurrence of NAFLD as of our study.

Conclusion

Patients who were previously labelled as cryptogenic cirrhosis of liver are now increasingly diagnosed as having underlying NAFLD. As most patients of NAFLD are asymptomatic, all diabetic cases especially obese subjects must undergo ultrasound study for early detection of change in echo texture when seen they must get their Liver enzymes must be tested to make an early diagnosis of NAFLD. If NAFLD detected early, treatment with reduction of weight, Exercise and dietary modification will held in reduction or even reversal of NAFLD in these Diabetics. Poor glycemic control had increased incidence of NAFLD good glycemic control must be achieved in all diabetics to prevent development of NAFLD.

References

1. Marchesini G, Marzocchi R, Agostini F, Bugianesi E. Non alcoholic fatty liver disease and the metabolic syndrome. Curr. Op in Lipidol. 2005;16:421-427.
2. Contos MJ, Sanyal AJ. The clinicopathologic spectrum and management of non-alcoholic fatty liver disease. Advances in anatomy and pathology. 2002;9:37-51.
3. Rakesh Gaharwar, Sushma Trikha, Shubha Laxmi Margekar, Om Prakash Jatav, P Deepak Ganga. Study of Clinical Profile of Patients of Non Alcoholic Fatty Liver Disease and its Association with Metabolic Syndrome. JAPI. 2015;63:12-16.
4. Williams KH, Shackel NA, Gorrell MD, McLennan SV, Twigg SM. Diabetes and nonalcoholic fatty liver disease: a pathogenic duo. Endocr Rev. 2013;34(1):84-129.
4. Bedogni G, Miglioli L, Masutti F, *et al*. Prevalence of and risk factors for nonalcoholic fatty liver disease: the Dionysos Nutrition and Liver Study. Hepatology. 2005;42:44-52.
5. Giovanni, *et al*. Prevalence of NAFLD and its association with cardiovascular disease among type 2 diabetic patients. Diabetes Care. 2007;30:1212-1218.
6. Agarwal AK, Vineet Jain, Sumeet Singla, Baruah BP, Vivek Arya, Rajbala Yadav. Prevalence of non-alcoholic fatty liver disease and its correlation with coronary risk factors in patients with type 2 diabetes. JAPI. 2011;59:351-354.
7. Matteoni CA, Younossi ZM, Gramlich T, *et al*. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology. 1999;116:1413-1419.
8. Reid AE. Nonalcoholic steatoepatitis. Gastroenterology. 2001;121:710-723.
9. Cortez-Pinto H, Baptista A, Camilo ME, De Moura MC. Nonalcoholic steatohepatitis-a long term follow up study: comparison with alcoholic hepatitis in ambulatory and hospitalised patients. Dig Dis Sci. 2003;48:1909-1913.