Original Research Article

A study of non-alcoholic fatty liver disease and its relation to type 2 diabetic patients and cardiovascular risk markers

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a unique entity characterised by fatty changes with lobular hepatitis in absence of a history of alcoholism. Compelling evidence over the past several years has substantiated a significant link between NAFLD and cardiovascular disease ranging from coronary artery disease to subclinical carotid atherosclerosis. Close follow up, treatment of risk factors for NAFLD, and cardiovascular risk stratification are necessary to predict morbidity and mortality in these patients. The objective of this study is to find out hepatic involvement in type 2 diabetic patients and to correlate the associations between non-alcoholic fatty liver disease and different Cardiovascular risk factors.

Methods: This prospective and observational study was conducted in a tertiary care Centre, Kolkata, West Bengal and was conducted among 128 patients having patients having been diagnosed as type 2 diabetic and whose liver USG scan showing fatty changes.

Results: In the studied 128 cases, 99 patients had fatty liver and 29 cases without fatty liver diagnosed by abdominal ultrasonography. Most of the Diabetic NAFLD cases were detected in their 5th and 6th decade of life with a male preponderance. Ultrasonography remains a reliable non-invasive method for detection. Ischemic changes in ECG were noted in the study population without statistical significance probably due to low sampling.

Conclusions: Left ventricular diastolic dysfunction found to be the prime echocardiographic abnormality in type 2 diabetes mellitus patients.

Keywords: Cardio-vascular risk, Non-alcoholic fatty liver disease, Type 2 diabetic

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the upcoming leading cause of chronic liver disease in the United States and its prevalence is increasing world-wide. It is a spectrum of liver diseases that ranges from simple steatosis to a progressive form of liver disease called nonalcoholic steatohepatitis (NASH). The prevalence of NAFLD is remarkably high in populations of both industrialized and developing countries, although there is variation depending on the criteria used and the population studied.[1] In one study of adults based on histological findings, mild to severe steatosis was shown in 70% of obese patients compared to 35% of lean patients. Steatohepatitis was found in 18.5% of obese patients, compared to 2.7% of lean patients.[2] In the primary care setting, NAFLD accounts for at least one third of cases of suspected chronic liver disease. Among patients with abnormal liver enzymes, NAFLD accounts for 40-80% of cases, with its prevalence strongly influenced by the presence of coexisting obesity, diabetes and dyslipidaemia.[3] In severely obese patients (usually

defined as BMI >35kg/m2), the prevalence of steatosis is over 90% from patients undergoing bariatric surgery.[4] From another perspective, three-quarters of type 2 diabetic patients have steatosis. The coexistence of diabetes in NAFLD patients more than doubles the prevalence of cirrhosis from 10-25%.[5] Among patients with hyperlipidemia, at least two-thirds with hypertriglyceridemia and one-third with hypercholesterolemia have fatty liver by ultrasonography.[6] Liver imaging may be a more reliable method for diagnosing NAFLD. In three large population studies, ultrasound imaging suggestive of NAFLD was independently associated with cardiovascular events.[7-9] Overall survival was reduced in subjects with NASH compared to the general population due to increased mortality by cardiovascular disease. Importantly in this study, only subjects with NASH had significantly reduced survival.[10-11] Several mechanisms have been postulated for development of accelerated atherosclerosis in patients with NAFLD, including genetic predisposition, insulin resistance and atherogenic dyslipidemia, oxidative stress, chronic inflammation, reduced levels of the adiponectin and altered production of pro and anticoagulant factors.[12] All these mechanisms are present at the same time. NAFLD, regardless of its stage, is strongly associated with hepatic and adipose tissue insulin resistance (IR). In fact, liver fat content can be used as an independent predictor of insulin resistance. These mechanisms work synergistically.[13] NAFLD, especially in its necro inflammatory form (NASH), may cause atherogenic dyslipidemia.[14]

The objectives of this study are to find out hepatic involvement in type 2 diabetic patients, to correlate the associations between non-alcoholic fatty liver disease and different cardiovascular risk factors and evaluation of non-alcoholic fatty liver disease as a component of metabolic syndrome.

METHODS

This study was a case series and of prospective and observational in nature. Study was conducted in a tertiary care Centre, Kolkata, West Bengal and was conducted among 128 patients having Patients having been diagnosed as type 2 diabetic and whose liver USG scan showing fatty changes.

The study was carried out during the period from August 2016 to July 2017. Study population was outdoor and indoor patients of type 2 diabetes mellitus. Study population was divided in three groups, according to the duration of the diagnosis of diabetes. Each group had at least 30 patients. Control group will consist of age matched 29 patients having type 2 diabetes without having evidence of fatty liver. Study method was Interview schedule questionnaire, OPD records, bedside tickets, physical examinations and laboratory measurements.

Study population was divided in three groups, according to the duration of the diagnosis of diabetes. Each group had at least 30 patients. Control group will consist of age matched 29 patients having type 2 diabetes without having evidence of fatty liver. The distributions of different groups are GROUP A- less than 5 years, GROUP B- in between 5 to 10 years and GROUP C- more than 10 years.

Inclusion criteria

Patients having been diagnosed as type 2 diabetic and Liver USG scan showing fatty changes (USG will be done in patients of diabetes as a routine investigation).

Exclusion criteria

Long term history for chronic alcoholism, known hepatic disease, HBS Ag or anti HCV positivity, history of ingestion of hepatotoxic drugs, blood for ANA positivity.

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5 % level of significance. The Statistical software namely SAS 9.2, SPSS 15.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Table 1: Age distribution.

Age distribution by hepatic status				
Age	**Status**		**Total**	**P-value**
	Fatty liver	Non-Fatty liver		
30-40	9 (7.03%)	5 (3.91%)	14 (10.94%)	
41-50	22 (17.19%)	8 (6.25%)	30 (23.44%)	
51-60	36 (28.13%)	12 (9.38%)	48 (37.5%)	
61-70	22 (17.19%)	3 (2.34%)	25 (19.53%)	0.4461
71-80	7 (5.47%)	1 (0.78%)	8 (6.25%)	
>80	3 (2.34%)	0 (0%)	3 (2.34%)	
Total	99 (77.34%)	29 (22.66)	128 (100%)	

In present study, authors have found most of the cases of fatty liver (28.03%) in the age range of 51-60 years group. There were 2.43% cases with fatty liver above 80 years age.

On the contrary, above 80 years age, had fatty liver in all of them (Table 1). Among the 77.34% fatty liver cases 40.63% was male and 36.72% was female. 5.05% patients did not show any left ventricular diastolic dysfunction. 44.44% showed type 1, 42.42% showed type 2, 8.08% showed type 3 diastolic dysfunction. Type 3 LVDD was found mostly (3.03%) in cases with duration of diagnosis >10 years group. (Table 2).

Table 2: Prevalence of LVDD with duration of diabetes.

Duration of diabetes	LVDD				Total	P-value
	0	1	2	3		
5-10 years	3	15	16	4	38	
	(3.03%)	(15.15%)	(16.16%)	(4.04%)	(38.38%)	
0-5 years	2	17	11	1	31	
	(2.02%)	(17.17%)	(11.11%)	(1.01%)	(31.31%)	0.4908
>10 years	0	12	15	3	30	
	0	(12.12%)	(15.15%)	(3.03%)	(30.3%)	
Total	5	44	42	8	99	
	(5.05%)	(44.44%)	(42.42%)	(8.08%)	(100%)	

25.78% subjects showed ischemic changes in their ECG. In the >10 years duration group showed 8.59% cases with ischemic changes in ECG. Statistical significance not found. (Table 3).

Table 3: Prevalence of ischemic changes in ECG with duration of diabetes.

Duration of diabetes	Ischemic changes in ECG		Total	P-value
	Absent	Present		
5-10	35	14	49	
	27.34	10.94	38.28	
0-5	36	8	44	
	28.13	6.25	34.38	0.35
>10	24	11	35	
	18.75	8.59	27.34	
Total	95	33	128	
	74.22	25.78	100	

Table 4: Prevalence of hypertension with hepatic status.

Status of liver	HTN			Total	P-value
	0	1	2		
Fatty liver	15	59	25	99	
	11.72	46.09	19.53	77.34	
Non-fatty liver	18	11	0	29	<0.001
	14.06	8.59	0	22.66	
Total	33	70	25	128	
	25.78	54.69	19.53	100	

46.09% cases with fatty liver showed grade 1, 19.53% showed grade 2 hypertension. Among the subjects without fatty liver, 8.59% showed grade 1but the control population did not show any grade 2 hypertension. P value was significant (Table 4).

29.79% cases were in the range of HbA1C>10%. Among them 4.26% cases showed Type 3 LVDD. Type 1 LVDD was prevalent in the range of 8.1-10%, type 2 LVDD in the range of 7.1-8%. P value was not significant (Table 5).

Table 5: Prevalence of LVDD with A1C in fatty liver.

A1C	LVDD				Total	P-value
	0	1	2	3		
6.4-7	2	9	4	2	17	
	2.13	9.57	4.26	2.13	18.09	
7.1-8	0	10	13	1	24	
	0	10.64	13.83	1.06	25.53	
8.1-10	0	13	11	1	25	0.2571
	0	13.83	11.7	1.06	26.6	
>10	1	10	13	4	28	
	1.06	10.64	13.83	4.26	29.79	
Total	3	42	41	8	94	
	3.19	44.68	43.62	8.51	100	

Table 6: PPBS by LVDD in fatty liver.

PPBS	LVDD				Total	P-value
	0	1	2	3		
≤200	11	6	9	0	26	
	8.59	4.69	7.03	0	20.31	
>200	6	54	34	8	102	<0.001
	4.69	42.19	26.56	6.25	79.69	
Total	17	60	43	8	128	
	13.28	46.88	33.59	6.25	100	

42.2% cases with PPBS>200 mg/dl showed type 1, 26.6% showed type 2, and 6.25% type 3 LVDD. P value was significant. (Table 6).

DISCUSSION

Liver ultrasonography results, although not sufficiently sensitive to detect liver inflammation and fibrosis, correlate well with the histological finding of fatty infiltration. In addition, international guidelines have been proposed for the diagnosis of different degrees of steatosis. NAFLD is associated with various metabolic abnormalities, including central obesity, type 2 diabetes, dyslipidaemia, high blood pressure, and metabolic syndrome (MetS). Fatty liver can develop as the result of various metabolic conditions that promote fat accumulation and inflammation in the liver. Otherwise, NAFLD may contribute to the development of MetS.

There is increasing evidence for an association between NAFLD and an increased risk of cardiovascular morbidity and mortality. The association between NAFLD and cardiovascular risk factors can largely explain the higher risk of cardiovascular disease among people with NAFLD.

The aim of this study was to assess the prevalence of fatty liver disease in known Type 2 diabetic cases and whether, these cases do have increased association of cardiovascular risk factors with them compared to the population with type 2 diabetes without fatty liver disease.

Banerjee S et al in their study showed fatty change in 43%, non-alcoholic steatohepatitis (NASH) could be identified in 40% with more advanced disease in 23% of the study population.[15] CRP is a potent cardiovascular risk factor. Chia-Hung Chiang et al established in their study that NAFLD patients have increased risk of CVD and elderly subjects have raised CRP value with a p value 0.004.[16] Authors have found significant association of hypertension with fatty liver disease in present study population as 46.09% cases showed grade 1 and 19.53% grade 2 hypertension. P value was significant. Present findings are supported by a study from Targher et al as they showed, 27.54% cases with grade 2 hypertension in study population with a odd ratio 1.42 with a significant p value.[17] Hypertensive patients were mostly associated with left ventricular hypertrophy as detected in present study (17.17%), p value was significant (Table 7) (p<0.001). According to Bleumke DA et al, abnormal left ventricular mass and geometry stands out to be potential marker of myocardial remodeling and cardiovascular disease.[18]

CONCLUSION

This study was done among the diabetic patients with fatty liver, to specifically assess the whole spectrum of disease, both from cardiovascular and metabolic perspective. Authors reviewed multiple studies across the globe in this respect. These studies established the association of different cardiovascular parameters in fatty liver patients, whether diabetic or non-diabetic. Authors

have found, quite the same results among present study population, who had association of multiple cardiovascular abnormalities, in comparison to the patients without fatty liver. Liver appears to be the window to the Heart. Authors studied 128 cases, among them 99 patients had fatty liver and 29 cases without fatty liver diagnosed by abdominal ultrasonography. Most of the Diabetic NAFLD cases were detected in their 5th and 6th decade of life with a male preponderance. Ultrasonography remains a reliable non-invasive method for detection.

Association of NAFLD with various physical and metabolic parameters like WHR, BMI, hyperlipidemia (hypertriglyceridemia specially), was proved beyond doubt and was found to be significantly associated with fatty liver disease when compared with age-matched control. CRP is found to be an independent coronary risk associate in Diabetic NAFLD patients.

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