

Non-Alcoholic Fatty Liver Disease and Metabolic Syndrome in Type 2 Diabetes Mellitus Patients in Rajshahi Medical College Hospital

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INTRODUTION

Non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome have become a public health problem worldwide due to rising incidence of obesity and Type 2 diabetes mellitus. NAFLD is a common liver disorder that is strongly associated with insulin resistance and Type 2 diabetes mellitus.

INTRODUCTION

Non-alcoholic fatty liver disease is characterised by excess deposition of fat in liver. This ranges from simple steatitis to steatohepatitis, cirrhosis and hepatocellular carcinoma (HCC) (Farrell and Larter, 2006). Hypertension, diabetes, obesity and dyslipidemia are predisposing factors of NAFLD (McCullough, 2006). These are also considered as components of metabolic syndrome. NAFLD is supposed to be hepatic manifestation of metabolic syndrome (Angulo, 2002, Day, 2006, McCullough, 2006, Marchesini et al., 2005).

INTRODUCTION CONT.

The prevalence of NAFLD in Type 2 DM patients is about 75% (Angulo, 2002) and Diabetes mellitus is observed in 18%–45% NAFLD patients (Browning et al., 2004, Weston et al., 2005). Compared with non diabetic subjects, people with type 2 diabetes have an increased risk of developing NAFLD and have a higher risk of developing fibrosis and cirrhosis (Angulo, 2002, Day, 2006, McCullough, 2006, Marchesini et al., 2005).

INTRODUCTION CONT.

Although about 70–75% of type 2 diabetic patient may have some form of NAFLD (Medina et al., 2004) precise prevalence of NAFLD in type 2 diabetes is unknown. To determined he prevalence of NAFLD in Diabetes patients is a burning issue in Bangladesh. Data on prevalence of NAFLD in diabetes patient is still lacking here. There are few studies of NAFLD in diabetic patients in world. Hence study is needed in the field to know proportion and clinical spectrum of NAFLD and metabolic syndome in diabetic patients in our country.

RATIONALE

Currently to the best of my knowledge, there is lack of local study on the prevalence of NAFLD and hence no local guideline is therefore available in its prevention, diagnosis and management. In addition results obtained from this study can be compared with results of other completed or ongoing studies from other regions of the world.

RESEARCH QUESTION

- 1. What is the proportion of Non-alcoholic fatty liver disease in Type 2 diabetes mellitus patient?
- 2. What is the proportion of metabolic syndrome in Type 2 diabetes mellitus patient?
- 3. What is the relationship between NAFLD & metabolic syndrome in type 2 DM patient?

STUDY OBJECTIVE

General Objective:

• To determine the proportion of NAFLD and metabolic syndrome in type 2 diabetes mellitus patients.

Specific Objectives

- To find out the proportion of NAFLD in patients with type 2 diabetes mellitus by ultrasonography.
- 2. To find out proportion of metabolic syndrome among type 2 diabetes mellitus patients with or without NAFLD.
- 3. To find out relationship between NAFLD and its severity with associated risk factors in type 2 diabetic patients.

METHODOLOGY

Study Type

: Cross sectional descriptive study.

Study Place

: Medicine inpatient and outpatient

department, Rajshahi Medical College Hospital

Study Period

:July,2015 – June,2017.

Study Population

: Type 2 DM patient

Sampling Procedure

: Purposive sampling method.

Sample Size

: 91 cases of Type 2DM patients.

Inclusion Criteria:

- 1. Patients of both sexes.
- 2. Patients diagnosed as type 2 diabetes mellitus.

Exclusion Criteria:

- 1. Persons with previous history of jaundice.
- 2. Patients with history of alcohol consumption.
- 3. Persons with history of chronic kidney disease and ischemic heart disease.
- 4. Patients with prior serologic evidence of HBV or HCV infection.

RESULTS

Table- 1 : Socio-demographic distribution of patients with type 2 DM (n=91)

		Frequency	%
	1. ≤45 years	6	6.5
	2. 46-55 years	68	75.0
Age	3. 56-65 years	10	11.0
	4. >65 years	7	7.5
	1. Male	61	67.0
Sex	2. Female	30	33.0
	1. Present	23	25.0
Smoking History	2. Absent	68	75.0
	1. Service holder	30	33.0
	2. Businessman	20	22.0
Occupation	3. Housewife	30	33.0
	4. Others	11	12.0
	1. Muslim	71	78.0
Religion	2. Non Muslim	20	22.0
	1. Below primary	11	12.0
Education	2. Up to HSC	30	33.0
	3. Graduate	50	55.0
N	1. <15000 Tk.	27	30.0
Monthly income	2. >15000 Tk.	64	70.0
Marital atatus	1. Married	82	90.0
Marital status $\frac{1}{x}$ +SD age = 51.43	2. Unmarried	9	10.0

In this study 75% of patients was in between 46-55 years of age with a mean age 51.43 ± 6.24 years and male female ratio was 2:1. Most of the patients with type 2 DM were non smoker (75.0%), normotensive (68.2%). 78% patient were Muslim, 90% patient were married, 70% patient had monthly income >15,000 taka, 33% patient were service holder, 33% patient were housewife and 22% were businessman, 55% patient were graduate.

Table-1: Clinical variables of metabolic syndrome in

		AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA		
at	ients with type 2 DM (n=91)	Frequency	%	Mean ±SD
BM	II			
1.	Normal(18.5-22.9 kg/m ²)	1	1.1	27.27±2.83
2.	Overweight (23.0-24.9 kg/m ²)	17	18.7	
3.	Obese (>25.0 kg/m ²)	73	80.2	
Wai	ist circumferance Normal (<90 cm in male, <80 cm in female)	32	35.2	102.22±8.01
2.	Increased (>90 cm in male, >80 cm in female)	59	64.8	102.22±0.01
HT	N			
1.	Present	29	31.8	
2.	Absent	62	68.2	

In this study 18.7% patient was overweight and 80.2% were obese. Increased WC was observed in 64.8% patient. 31.8% were hypertensive.

Table-2: Lipid profile of patients with type 2 DM (n=91)

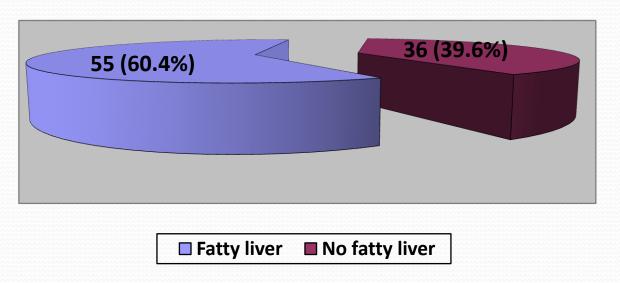
		Frequency	%	Mean ±SD
HD	L			
1.	Low (<40 mg/dl in male, <50 mg/dl in female)	8	8.8	41.85±2.72
2.	Normal (>40 mg/dl in male, >50 mg/dl in female)	83	91.2	
TG				
1.	Normal (<150 mg/dl)	25	275	186.08±58.42
2.	High (≥150 mg/dl)	66	72.5	
LD	L			
1.	Optimal (<100 mg/dl)	49	54.0	
2.	Near optimal (100-129 mg/dl)	18	20.0	
3.	Borderline high (130-159 mg/dl)	6	6.5	
4.	High (160-189 mg/dl)	11	12.0	
5.	Very high (≥190 mg/dl)	7	7.5	
Tot	al cholestrol			
1.	Desirable (<200 mg/dl)	61	67.0	
2.	Borderline high (200-239 mg/dl)	19	21.0	
3.	High (≥240 mg/dl)	11	12.0	

Table-3: Duration and control of diabetes mellitus in patients with type 2 DM (n=91)

	Frequency	%	Mean±SD
Duration of DM			
1. 0-4 years	23	25.0	
2. 5-9 years	32	35.0	
3. >9 years	36	40.0	
Control of DM			7.44±4.21
1. Controlled	29	31.8	
2. Uncontrolled	62	68.2	

In this study (35.0+40.0)% patients had diabetes more than 5 years and majority (68.2%) of patient DM was uncontrolled.

Figure-1: Proportion of fatty liver in patients with type 2 DM by abdominal ultrasonography (n=91).



In this study ultrasonographic proportion of NAFLD was 60.4% in patients with type 2 DM.

Table-4: Relationship between NAFLD and age of patients with type 2 DM (n=91).

	Ultrasonographic e	χ^2 test	
	Present (n=55) Absent (n=36)		(p value)
	no(%)	no(%)	
Age group			
1. ≤45 years	2(33.3)	4(66.7)	
2. 46-55 years	39(57.4)	29(42.6)	0.069
3. 56-65 years	7(70.0)	3(30.0)	
4. >65 years	7(100)	0(0.0)	
Total	55(60.4)	36(39.6)	

Table-5: Relationship between NAFLD and sex of the patients with type 2 DM (n=91).

	Ultrasonographic e	χ^2 test	
	Present (n=55) Absent (n=36)		(p value)
	no(%)	no(%)	
Sex			
1. Male	36(59.0)	25(41.0)	0.692
2. Female	19(63.3)	11(36.7)	
Total	55(60.4)	36(39.6)	

In this study 59% male and 63.3% female had ultrasonographic evidence of NAFLD. So almost similar proportion of NAFLD was found in both male and female ($\chi^2 = 0.157$, df=1, p=0.692).

Table-6: Relationship between NAFLD and duration of DM in patients with T2DM (n=91)

Duration of DM	Ultrasonographic evidence of fatty liver		χ^2 test
	Present (n=55) no(%)	Absent (n=36) no(%)	(p value)
1. 0-4 years	11(47.8)	12(52.2)	<0.01
 5-9 years >9 years 	15(46.9) 29(80.6)	17(53.1) 7(19.4)	
Total	55(60.4)	36(39.6)	

Increased duration of DM was significantly associated with higher proportion of NAFLD ($\chi^2=10.086$, df=2, p<0.01).

Table-7: Relationship between NAFLD and presence of HTN in patients with type 2 DM (n=91)

	Ultrasonographic e	vidence of NAFLD	χ^2 test
	Present (n=55)	Present (n=55) Absent (n=36)	
	no(%)	no(%)	
HTN			
1. Present	20(68.9)	9(31.1)	0.255
2. Absent	35(56.5)	27(43.5)	
Total	55(60.4)	36(39.6)	

HTN was not significantly associated with higher proportion of NAFLD ($\chi^2=1.294$, df=1, p=0.255).

Table-8: Relationship between NAFLD and BMI patients

with type 2 DM (n=91)

Ultrasonographic evidence of

 χ^2 test

	NAF	(p value)	
	Present (n=55)	Absent (n=36)	
	no(%)	no(%)	
BMI			
1. Normal (18.5-22.9 kg/m ²)	0(0)	1(100)	
2. Overweight (23-24.9 kg/m ²)	1(5.9)	16(94.1)	< 0.001
3. Obese (>25 kg/m ²)	54(73.9)	19(26.1)	
Total	55(60.4)	36(39.6)	

• Obesity was significantly associated with higher proportion of NAFLD in patients with type 2 DM (χ^2 =28.282, df=2, p=<0.001).

Table-9: Relationship between NAFLD and waist circumferance in patients with type 2 DM (n=91)

	Ultrasonograpl	χ^2 test	
	NAI	NAFLD	
	Present (n=55)	Absent (n=36)	
	no(%)	no(%)	
Waist circumference			
1. Normal (<90 cm in male, <80 cm in female)	10(31.3)	22(68.7)	< 0.001
2. Increased (>90 cm in male, >80 cm in female)	45(76.2)	14(23.8)	
Total	55(60.4)	36(39.6)	

• So increased waist circumference was significantly associated with higher proportion of NAFLD in patients with type 2 DM ($\chi^2=17.588$, df=1, p=<0.001).

Table-10: Relationship between NAFLD and HDL level in patients with type 2 DM (n=91)

	Ultrasonographic evidence of NAFLD		χ^2 test
	Present (n=55)	Absent (n=36)	(p value)
	no(%)	no(%)	
HDL			
1. Low (<40 mg/dl in male, <50	8(100)	0(0)	< 0.05
mg/dl in female)	47(56.6)	36(43.4)	
2. Normal (>40 mg/dl in male,			
>50 mg/dl in female)			
Total	55(60.4)	36(39.6)	

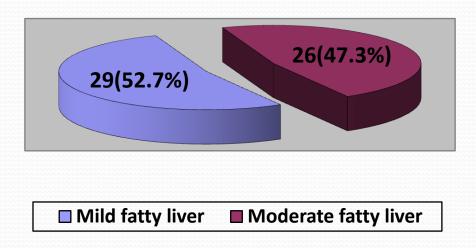
In this study 100% patient with low HDL level had NAFLD. So all patients with low HDL was found to have NAFLD and it is statistically significant (χ^2 =5.741, df=1, p=<0.05).

Table-11: Relationship between NAFLD and TG level in patients with type 2 DM (n=91)

	Ultrasonographic ev	vidence of NAFLD	χ^2 test
	Present (n=55)	Absent (n=36)	(p value)
	no(%)	no(%)	
TG			
1. Normal (<150 mg/dl)	10(40.0)	15(60.0)	< 0.05
2. High (≥150 mg/dl)	45(68.2)	21(31.8)	
Total	55(60.4)	36(39.6)	

In this study 68.2% patient with high level of TG had ultrasonographic evidence of NAFLD. Higher TG level was significantly associated with higher prevalence of NAFLD (χ^2 =6.023, df=1, p=<0.05).

Figure-2: Severity of NAFLD on basis of Ultrasonography in patients with type 2 DM (n=55)



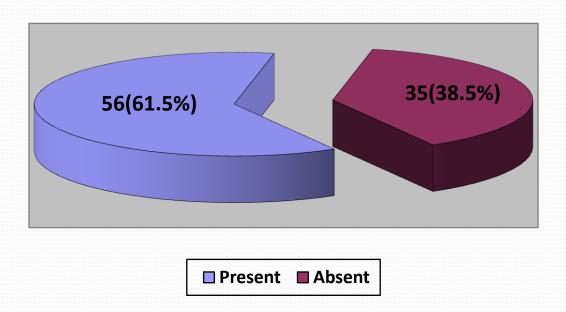
In this study 29 (52.7%) had mild fatty change in liver and 26 (47.3%) had moderate fatty change in liver on ultrasonography in patients of T2DM with NAFLD.

Table-12: Relationship between severity of NAFLD and DM control in patients with type 2 DM (n=55)

	Severity of NAFLD		χ^2 test
	Mild (n=29)	Moderate (n=26)	(p value)
	no(%)	no(%)	
DM control			
1. Controlled	12(92.3)	1(7.7)	
2. Uncontrolled	17(40.5)	25(59.5)	< 0.01
Total	29(52.7)	26(47.3)	

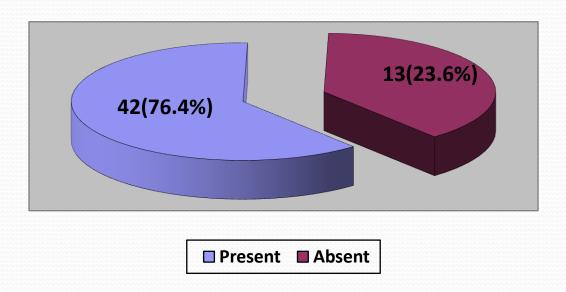
In this study 40.5% patient with uncontrolled DM had mild and 59.5% patient with uncontrolled DM had moderate form of NAFLD. So uncontrolled DM was significantly associated with more severe NAFLD ($\chi^2=10.700$, df=1, p=<0.01).

Figure 3: Proportion of metabolic syndrome in patients with type 2 DM (n=91)



In this study proportion metabolic syndrome in patients with type 2 DM was 61.5%.

Figure 4: Proportion of metabolic syndrome in patients with type 2 DM with NAFLD (n=55)



In this study proportion of metabolic syndrome in patients with type 2 DM with NAFLD was 76.4%.

Table-13: Relationship between NAFLD and metabolic syndrome in patients with T2DM (n=91)

Metabolic syndrome	Ultrasonographic evidence of fatty liver		χ^2 test
	Present (n=55)	Absent (n=36)	(p value)
	no(%)	no(%)	
1. Present	42(75.0)	14(25.0)	< 0.001
2. Absent	13(37.2)	22(62.8)	
Total	55(60.4)	36(39.6)	

In this study 75.0% patient with ultrasonographic evidence of NAFLD had metabolic syndrome. Metabolic syndrome was significantly associated with NAFLD in patients with T2DM (χ^2 = 12.910, df=1, p<0.001).

DISCUSSION

Proportion of NAFLD and metabolic syndrome were 60.4% and 61.5% respectively. Mild fatty change was seen in 52.7% and 47.3% had moderate fatty change. 80.2% study population was obese, 31.8% was hypertensive and 72.5% had hypertriglyceridemia. Females were more affected than male. NAFLD was proportionately increased in higher age group but age and gender were statistically insignificant (p>0.05).

DISCUSSION

Long standing, uncontrolled diabetes, increased triglyceride and low HDL level were significantly associated with higher proportion and severe form of NAFLD (p<0.05). Increased BMI, waist circumference and metabolic syndrome were also significantly associated with NAFLD (p<0.05) but hypertension had no significant association (p>0.05). AST, ALT, AST:ALT ratio were within normal limit among study population.

CONCLUSION

Patients with type 2 DM are at increased risk for developing NAFLD when compared to general population. Patients with established type 2 DM should be screened for NAFLD to avoid diabetes worsening and associated chronic liver disease.

RECOMMENDATIONS

- 1. We recommend routine hepatic ultrasonography and LFTs monitoring in type 2 DM patients. Subsequently any patient found to have NAFLD should be reassessed periodically to prevent any early complication.
- 2. We recommend liver biopsy in diabetic patients with ultrasonographic evidence of fatty liver and a BAAT score ≥2 for histological profiling, as proposed by Laurin (2002).

RECOMMENDATIONS

- 3. Intensive modification of associated risk factors has been shown to improve hepatic histology in affected patients. So we recommended to take necessary steps to raise awareness among T2DM patients for strict control and also to control associated risk factors as well.
- 4. The need for vigilance and management of prevalent risk factors for NAFLD in patients with type 2 DM is important, as this may delay onset or progression of NAFLD.

LIMITATIONS

- 1. This was a single centre study and small number of sample was not sufficient to generate the findings.
- 2. There were more follow up patients than new patients attending medicine department, Rajshahi medical college hospital.
- 3. It was not possible to completely rule out previous use of medications that could cause secondary fatty liver disease.
- 4. Subjects did not have a liver biopsy and histological examination. We used ultrasound to detect fatty liver in our study.

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