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ORIGINAL ARTICLE

Non-alcoholic fatty liver in Type 2 Diabetes Mellitus study of factors responsible for it in a teaching hospital of Rohelkhand region(U.P.)

Amit Sachan*, Priyanka Sachan**, AB Mowar***, Smita Gupta***,MPRawal***, Nirmal Yadav****, Pranesh Nigam*****, *Jr. Resident 3rd year, Medicine,**Jr. Resident 3rd year, Pathology,***Assistant Professor of Medicine, ****Professor and Head of Medicine, *****Professor of Medicine

Department of Medicine, SRMS Institute of Medical Sciences, Nainitital Road, Bareilly,U.P.

Mailing Address: amit.sachan.pbt@gmail.com, Permanent Address: 221, Bagh Gulsher Khan, Pilibhit-262001

Abstract : *The morbidity and mortality in patients with type 2 Diabetes Mellitus(T_2DM) is related to non-alcoholic fatty liver disease(NAFLD) and its complications. Various factors including insulin resistance are responsible for the development of fatty liver. The present study is aimed to study the various factors responsible for NAFLD in T_2DM.*

Material and Method : *Patients with T_2DM were studied for the prevalence of NAFLD during one year at the tertiary referral center SRMS IMS, Bareilly. Patients with characteristic finding on ultrasonography were considered as having fatty liver. They were thoroughly interrogated for clinical history and physical examination and submitted to relevant laboratory investigations.*

Results : *Of the 90 patients of T_2DM, 82 patients (91.2%) had evidence of fatty liver. Serum transaminase and alkaline phosphatase levels were raised in across (10%) indicating liver damage.BMI(74 cases or 82.2%) and serum lipids,specially cholesterol and triglyceride(80 cases or 88.8%) were significantly higher. Duration of diabetes and blood sugar levels were directly proportionate to incidence of fatty liver. Glycosylated hemoglobin level indicate the control of diabetes and most of the cases had glycosylated hemoglobin more than 8%(72cases or 80%).*

Conclusion : *Fatty liver is a common finding among T_2DM patients. The factors responsible for it are duration and poor control of diabetes, obesity and dyslipidemia; Fatty liver can be prevented if all these provocative factors are controlled.*

Keywords: *Non-alcoholic fatty liver, Type 2 Diabetes, Dyslipidemia, Obesity, Body Mass Index.*

Non-Alcoholic Fatty Liver in Type 2 Diabetes Mellitus Studyof Factors Responsible for It in A Teaching Hospital in theRohelkand Region

Non-alcoholic fatty liver disease (NAFLD) is commonly associated with obesity, diabetes mellitus type 2,and dyslipidemia and insulin resistance components of the metabolic syndrome. Diabetes mellitus (DM) can alter hepatic morphology and physiology and DM can be precipitated by hepatic disorders[1]. NAFLD is increasingly being recognized as an important and common condition associated with DM. The spectrum can extend from clinical near normal or simple hepatic steatosis to non alcoholicsteatoheaptitis (NASH), cirrhosis (often accompanied by steatosis) and even hepatocellular carcinoma[2]. NASH is supposed to be a more severe part of NAFLD that can lead to cirrhosis, terminal liver failure and even carcinoma. Various studies have shown that NAFLD patients have higher mortality rate and lower survival than the general population[3-5]. NAFLD is associated with many factors including the presence of

type 2 DM which can increase its risk and severity[4,5]. Peripheral insulin resistance is a central mechanism in the pathogenesis of both entities[5,6].

Not surprisingly, 10-75% of NAFLD patients have T_2DM and 21-71% of patients with diabetes are reported to have NAFLD[5-7]. The mortality rate of diabetes due to hepatic disorders are more than twice the general population and patients with both NAFLD and DM have poorer prognosis.[3,8]. The present study was designed to determine the prevalence of NAFLD, its clinical spectrum and risk factors for the occurrence of severity of NAFLD and NASH.

Material and Methods

Ninety consecutive patients of proved type 2 DM according to WHO Guideline of 20 years and above age were included in this study to find out the prevalence of NAFLD and various risk factor. They were also non-alcoholic and having at least one year history of T2DM and on hypoglycaemic drugs and not on insulin therapy. Exclusion criteria included history of chronic liver disease of any etiology, malignancy and intake of medication known to cause the fatty liver.

A through medical history and physical examination were performed on every patient along with measurement of height and weight, BMI was calculated to measure obesity waist/hip ratio as an index of splanchnic fat accumulation[5,9]. After an overnight fast the serum was obtained from all patient for liver function test, serum enzyme(SGOT, SGPT and alkaline phosphate), serum lipid profile , blood sugar fasting and Glycalated haemoglobin(HbA_1c).

Abdominal ultrasonography was performed for evidence of fatty liver and evidence of other disease. Based on ultrasonographic finding patient were categorised as

Table: 1. NAFLD and its relation to obesity and dyslipidemia (n=90)

Parameters	With NAFLD n-82 No. of cases in%	Without NAFLD n-8 No. of cases in %	Total n=90 No. of cases in %
BMI (kg/m2)	27.8+/-4.26	22.9+/-3.9	28.4+/-8.6
23-24.9	26-31.7%	2-25%	28-31.1%
>25	44-53.6%	2-25%	46-51.1%
Waist circumference	102.6+/-14.2	86.2+/-6.8	98.2+/-6.8
91-100	12-14.7%	4-50%	16-17.7%
>100	57-69.5%	1-12.5%	58-64.5%
Waist hip ratio	1.28+/-0.28	0.86+/-0.3	1.18+/-0.48
0.9001-1.000	23-26.8%	2-25%	23-25.5%
1.0001-1.1000	24-29.3%	1-12.5%	25-27.7%
>1.1001	30-36.5%	-	30-41.1%
S.cholesterol level	264.6+/-9.2	216+/-7.2	254.2+/-10.27
200.1-250mg%	20-24.1%	3-37.5%	23-25.5%
>250mg%	57-69.5%	-	57-63.3%
S. triglyceride level	298.6+/-16.8	148+/-7.8	256.2+/-10.2
150.1-200mg%	6-7.3%	1-12.5%	7-7.8%
200.1-250mg%	11-13.4%	1-12.5%	12-13.3%
250.1-300mg%	11-13.4%	1-12.5%	12-13.3%
>300mg%	49-59.1%	-	49-54.4%
Serum LDL level	148.2+/-9.6%	98.6+/-4.5%	138.6+/-10.2%
100.1-125mg%	6-7.3%	1-12.5%	7-7.7%
125.1-150mg%	13-15.8%	-	13-14.4%
150.1-175mg%	21-25.4%	-	21-23.3%
>175mg%	33-40.2%	-	33-36.6%
Serum HDL	48.6+/-9.8	62.8+/-7.8%	51.8+/-9.6%
<40mg	35-42.6%	-	35-38.8%
40.1-50mg%	20-24.3%	1-12.5%	21-23.3%
50.1-60mg%	15-18.3%	1-12.5%	16-17.7%

those of with NAFLD and those without NAFLD.

Patient were analysed using SPSS 13.0 statistical software package for windows. Descriptive statistics were performed on all study parameter i.e. meanstandard deviation and range, chi. Square test.

Observation and Results

Ninety consecutive cases of Type 2 Diabetes Mellitus(T_2DM) of age varying from 35 to 86 years with mean ± SD 55.96 ±11.65years(54 males and 36 femaleswith male to female ratio 1.5:1) were included in this study.A large proportion of cases were obese and dyslipidemic (53.6% and 64.5%; BMI >23kg/m^2 and serum triglyceride >150mg%). The prevalence of obesity (BMI >25kg/m^2) in patient with NAFLD was 53.6% as compared to 25.0% in non-NAFLD patient.

The central obesity (measured by waist circumference and waist - hip ratio) was none as NAFLD patients(Table 1). The waist circumference >100cm was more in NAFLD(69.5%) patient as compared to non-NAFLD(12.5%). The same was also in waist-hip ratio which was more the 1.000 in 65.8% in NAFLD. Hyperlipidemia was also higher in NAFLD patients.The serum cholesterol level were above 250 mg% in 69.5%, serum triglyceride >250 mg% in 72.5% and LDL >125% in 41.2% of cases of NAFLD and the HDL was less the <50% in 66.9% of cases of NAFLD.

As depicted in Table 2 the NAFLD occurrence was related to duration and severity of diabetes. Incidence was more in patients with duration of diabetes more than 5 years(94%) period. Fasting blood sugar >126mg%(58.4%) post prandial blood sugar above 180 mg %(75.5 %) and glycosylated haemoglobin HbA_1c >8.0% (84.2%) were raised in patients with NAFLD.

Serum enzymes			
AST(IU%)	36.2+/-8.5	20.4+/-5.6	35.8+/-9.2
>40 (mean+/-SD)	8-9.7%	1-12.5%	9-10%
ALT(IU%)	34.2+/-10.2	-	34.9+/-10.2
>40(mean+/-SD)	7-8.5%	-	7-7.7%
Alk. Phoshatase	164.8+/-43.8	162.8+/-10.2	165.8+/-42.8
>150	9-10.9%	1-12.5%	10-11.1%
AST/ALT ratio	1.02+/-0.37	0.92+/-0.2	1.02+/-0.37

Discussion

In the present series of 90 cases of T_2DM there were 82 cases(91.1%) with NAFLD. In the literature there is very wide variation of incidence of NAFLD in T_2DM(21-78% or more)[5,7]. Males predominate the series(60%) with male to female ratio of 1.5:1. Merat et al[5]have found no significant(p=0.69) difference between the two sexes. Some studies reported higher incidence of NAFLD amongst females[10] whereas most studies reported the more prevalence among males diabeties[7,11-13]. The mean age of patients both the NAFLD and non- NAFLD was 55.96±11.86 years and 56.9±10.8 years respectively which was insignificant. NAFLD can occur in any age group but since its prevalence increases with age and mostly affects people in their forties to sixties as we observed too(Table 2)[5,10,12,13]. Merat et al[5] observed the mean duration of illness was significantly lower

Table 2: *Age and sex distribution of cases (n=90)*

Age group in years	Cases with NAFLD N = 82	Cases without NAFLD N = 8	Total % N = 90
21-40	2-2.68%	1-12.5%	3-3.5%
41-50	33-40.2%	2-25%	35-38.8%
51-60	22-26.8%	2-25%	24-26.6%
≥60	25-30.4%	3-37.5%	28-31.1%
Total	82-91.2%	8-8.8%	90-100%
Males	50-92.6%	4-50.2%	54-60%
Females	32-88.8%	4-50.2%	36-40%
Minimum age(years)	35	36	35
Maximum age(years)	86	84	86
Mean ± SD	55.96 ± 11.86	56.9 ± 8 yrs	54.2 ± 9.8

in patient with NAFLD (8.6±6.3years) as compared to patients without NAFLD(12.3±8.6years p-0.002). We too found significantly more number of patient of NAFLD with duration of diabetes less than 5 years(15 cases) as compared to cases without NAFLD(5 cases). We observed that incidence of NAFLD increases with increase in duration of diabetes(Table 3). This too is also described in literature i.e. duration of diabetes is directly proportional to duration of diabetes.[11-13]

There was no significant difference in HbA_1C between the two groups but as HbA_1C increases there is proportionate increase in NAFLD patients. The same is evident in blood sugar levels i.e. blood sugar level both fasting and postprandial is directly proportional to NAFLD. It is because the altered glucose metabolism affects the fat metabolism leading to dyslipidemia which results in raised level of cholesterol, triglyceride, LDL and VLDL. These raised components affects the liver leading to NAFLD[5,9,13].This we observed in the present series of cases. This is also related to obesity. The NAFLD cases had raised BMI i.e.25kg/m^2 and waist circumference and waist hip ratio.[5,10]. We observed BMI was significantly higher in patients with NAFLD(mean= 27.8±4.26kg/m^2). Waists circumference and waist hip ratio was also higher in patients with NAFLD (102.6±14.2cm and 1.28±0.28 respectively). Many studies observed the obesity is the most common entity associated with NAFLD[5,10-13]. This ratio reflects abdominal(truncal) fat distribution and it has been shown in previous studies that there is a significant correlation between waist hip ratio and the degree of hepatic steatosis, even in the patients with normal BMI.[14]

Though we have not studied the insulin resistance in the present series of cases but as our subjects were all diabetics and we have diagnose the NAFLD on the basis of ultrasonographically, there will be up to some extent insulin resistance as well as increased insulin secretion. But several studies reported that insulin resistance did not appear to be an important factor in the development of NAFLD[5,7,9,11]. Kassler et al[5] showed that prevalence of NAFLD, as diagnosed by ultrasound was significantly higher in patient with acute myocardial infarction and is a dependable and reliable diagnostic method with sensitivity varies from 89% to 93%[5,16].

Dyslipidemias are commonly associated with NAFLD and studies have shown that 20-92% of patients diagnosed with NAFLD have hyperlipidemia including hypertriglyceridemia, hypercholesterolemia.[15]

Our figures of NAFLD in T_2DM were high as reported in several studies. Due to the significant rate of increased liver related morbidity and mortality in T_2DM patients

Table 3: NAFLD in relation duration and severity of diabetes (blood sugar levels)

Parameters	Cases with NAFLD N =82	Cases without NAFLD N=8	Total n= 90
Duration of diabetes (mean ± sd)	13.8 ± 7.8 years	7.9 ± 6.9 years	13.6 ± 9.6 years
<5	15-18.4%	3-37.5%	20-22.2%
6-10	28-34.1%	4-50%	30-33.3%
11-15	24-29.2%	1-12.5%	25-27.7%
>10	15-18.4%	-	15-16.6%
Fasting Blood sugar level(mg%)	162.5 ± 7.8	155.2 ± 7.2	164 ± 9.2
126-176	24-29.2%	4-50%	28-31.1%
176-226	12-14.6%	1-12.5%	13-14.5%
>226	12-14.6%	-	12-13.2%
P.P.B. sugar (mg%)	236.8 ± 24.2	196.8 ± 9.8	228.6 ± 42.5
181-230	34-41.4%	4-50%	38-42.2%
231-280	12-14.6%	-	12-13.22%
>280	16-19.5%	-	16-17.7%
HbA1c %	10.26 ± 5.6	7.92 ± 4.8	10.36 ± 9.8
6.6-8	8-9.7%	2-25%	10-11.5%
8.1-9.5	11-13.4%	1-12.5%	12-13.2%
9.6-11	15-18.2%	1-12.5%	16-17.7%
11.1-12.5	18-21.9%	1-12.5%	19-21.1%
>12.5	25-30.7%	-	25-27.7%

it is now essential to diagnose NAFLD at the earliest possible and treat accordingly to prevent the NAFLD. Unfortunately with the possible exception of weight reduction in obese there is no established treatment of NAFLD. The use of insulin sensitizers, anti-oxidants and other agents have been advocated in the treatment with success[4,5,12] but effective treatment is yet to come.

The present study concluded that it will lead to high prevalence of NAFLD is high amongst T_2DM patients and considering the increased liver morbidity and mortality among T_2DM patients. NAFLD should be actively find out and treat them. Ultrasonography for diagnosing NAFLD should be taken as reliable and dependable tool in diagnosing NAFLD.

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Education is the most powerful weapon which you can use to change the world.
– Nelson Mandela