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NON-ALCOHOLIC FATTY LIVER DISEASE -'A RISK FACTOR FOR CAD IN T_2DM'

Biochemistry

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ABSTRACT

Introduction: Non Alcoholic fatty liver disease (NAFLD) is a variety of hepatic steatosis, caused in abscene of excessive alcohol consumption. Obesity, Type 2 diabetes, and hyperlipidemia are regarded as risk factors for NAFLD which is also linked with insulin resistance. Data also suggests that NAFLD is as an independent risk factor of cardiovascular disease. So, It becomes pertinent to define cardio-metabolic factors associated with the presence of NAFLD in Indian diabetic patients.

Aim: To demonstrate the association of NAFLD with cardiometabolic risk factors in type 2 DM subjects.

Material & Methods: The present case control study consisted of 60 T_2DM patients with NAFLD (ultrasound examination)60 Type 2 DM patients without NAFLD (Non NAFLD) of age >35 years.

BMI was calculated as measure of obesity. Blood samples taken were analysed for FBS, HbA1c, lipid parameters(Tot. chl, LDL-C,HDL-C,TG) and transaminases(ALT and AST).

Result:BMI, FBS, HbA1c ($p<0.0001$,0.24,<0.000resp.) and lipid parameters ($p<0.0001$,0.004,0.0003<0.0001 resp.) show significant comparative values in NAFLD group. Whereas transaminases show non significant values.

Conclusion: NAFLD is associated with several cardiometabolic risk factors for CAD So, the present study stresses the need for early screening of NAFLD in type 2 Diabetes.

KEYWORDS

Non Alcoholic fatty liver disease, T2DM, BMI, cardiometabolic.

INTRODUCTION

Non Alcoholic fatty liver disease (NAFLD) is a variety of hepatic steatosis, caused in abscene of excessive alcohol consumption (a threshold of <30 g/day for men and <20 g/day for women)[1]. The prevalence of NAFLD has been reported as 50–87.1% in Type 2 Diabetics and 15-20% in general population[2]. Over the last two decades, the increasing prevalence of NAFLD have been paralleling with the rapidly progressing epidemic of obesity and type 2 diabetes[3].

Modernization of dietary habits and adoption of a sedentary lifestyle are associated with increasing prevalence of NAFLD in developing nations. NAFLD is regarded as the most common liver disorder in developed countries[4]. It is probably due to the contemporary epidemic of obesity and associated metabolic complications. Obesity, Type 2 diabetes, and hyperlipidemia are regarded as risk factors for NAFLD which is also linked with insulin resistance. It may, however, respond to life style modification leading to weight loss and insulin sensitizers drugs like metformin and thiazolidinediones and GLP-1 receptor agonists[5].

By present trends, India has been predicted to face an epidemic of NAFLD & T_2DM in future, Data also suggests that NAFLD is as an independent risk factor of cardiovascular disease, the commonest cause of mortality in such patients. So, It becomes pertinent to define cardio-metabolic factors associated with the presence of NAFLD in Indian diabetic patients. In otherwords, NAFLD can be regarded as hepatic manifestation of metabolic syndrome. So, the present study is directed to find the association between NAFLD and CAD in type 2 DM patients.

AIM OF THE STUDY

To demonstrate the association of NAFLD with cardiometabolic risk factors in T_2DM subjects.

MATERIAL AND METHODS

A case control study was conducted in the department of Biochemistry, VIMS, Pawapuri, Nalanda from June2020 to December 2020. 120 patients of both sexes with T_2DM of age >35 years attending the MOPD were divided into two groups each containing 60 patients.

The study was approved by the institutional ethical committee.

GROUP 1- T_2DM patients with NAFLD (ultrasound examination)
GROUP 2- T_2DM patients without NAFLD (Non NAFLD).

A detailed history taking along with complete physical examination was done. BMI was calculated as a measure of obesity.
Each of them was screened for
(I) CAD
- by any past H/O of CAD
-ECG or angiography evaluation
(ii) NAFLD - USG evidence of fatty changes in liver.

Serum obtained from blood sample(from anticubital vein) was analysed for FBG, HbA1c and Lipid profile(Tot. chl., HDL, LDL, TG), liver enzymes ALT and AST on Erba 200 automated analyser in Dept. of Clinical Biochemistry.

INCLUSION CRITERIA:

-All T2DM patients fufiling the ADA criteria
or
- already on treatment for DM.

EXCLUSION CRITERIA:

-acute or chronic viral hepatitis,
-h/o alcoholism,
-h/o drugs leading to steatosis (steroids, estrogens, tamoxifen, amiodarone, valproic acid, diltiazem, or methotrexate),
- h/o any other chronic liver disease.
-patients already on statins, or pioglitazones

STATISTICAL ANALYSIS

The continuous variables were expressed as means and standard deviations. Statistical analysis was performed with Graph pad Prism 5.0 statistical software. Independent student's t-test was applied for comparision of data between the two groups. Correlation of BMI and TG was analysed using Pearson's correlation coefficient.

Results of the study were discussed at 95% confidence interval; interpretation of the test results was done according to p value ($P<0.05$ - significant and $P\geq0.05$ - not significant).

RESULT

The present case control study consisted of 60 diabetic patients with NAFLD, that were compared with 60 non NAFLD diabetic patients of the same age group and sex. Group I consisted of 58.3% of males as the majority while group II includes 51.6% females as majority (Figure 1).

Table 1 shows comparison of variables between group I and group II. The mean age of the NAFLD diabetic subjects was 56.61±6.7 years while that of the non NAFLD was 53.73±8.25 years,(significant, p= 0.03). BMI was significantly elevated in group I with p <0.0001. FBS was also significantly raised, (p = 0.024) in NAFLD diabetics. HbA1c was again significantly (p<0.0001) raised in NAFLD group. Serum total cholesterol was also significantly raised (p<0.0001) in NAFLD group. Similarly, LDL-C and TG show significant increase (p=0.004,p<0.0001 resp.) in group I. While Serum HDL-C in group I patients was found to be 41.21 ± 8.02 mg/dl which was significantly lower (p=0.0003) than that of the group II (46.82 ± 9.44 mg/dl). Transaminases show non significant values(p=0.38,p=0.63 resp.)

Figure 2 shows significant positive correalation between BMI and TG (r=0.6595,p<0.0001).

Figure 3 shows prevalence of CAD in both the groups which was higher(30%) in NAFLD group.

1: Comparison of characteristics of Type 2 Diabetes mellitus patients with and without NAFLD

Variables	T_2DM with NAFLD	T_2DM without NAFLD	t value	P value
Age (years)	56.61± 6.7	53.73±8.25	2.093	0.03
BMI (kg/m^2)	27.04±2.6	23.31±1.37	9.575	<0.0001
FBS (mg/dl)	110.46±24.30	102.16±14.22	2.283	0.024
HbA1c	7.9±2.12	6.6±0.59	4.670	<0.001
Total cholesterol (mg/dl)	206.27±44.15	136.48±28.64	8.685	<0.0001
LDL-C (mg/dl)	156.18±43.82	91.1±19.76	2.914	0.004
HDL-C (mg/dl)	41.21±8.02	46.82±9.44	3.731	<0.005
TG (mg/dl)	204.49±44.15	129.98±32.63	10.512	<0.0001
ALT(IU/L)	40.78±10.42	39.08±10.80	0.877	0.382 (NS)
AST(IU/L)	35.06±9.06	36.40±9.31	0.476	0.63 (NS)

NS: Non Significant

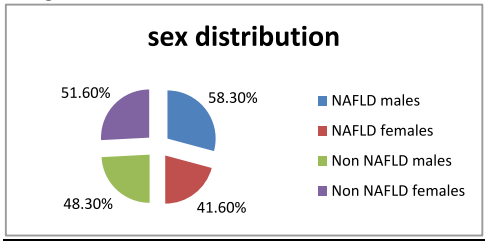

Figure 1: Sex wise distribution of patients

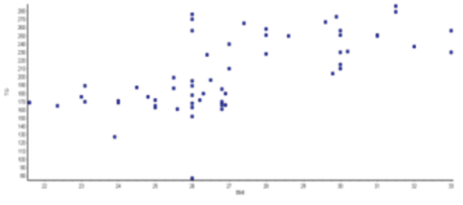

Figure 2: Correlation between TG and BMI

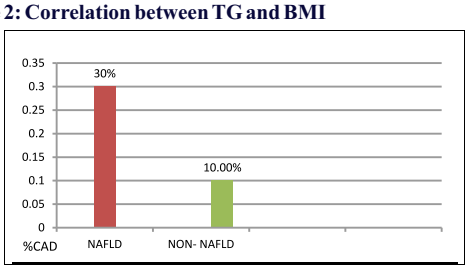

Figure 3: Prevalence of CAD in T_2DM

DISCUSSION

In our study, mean age (56.61± 6.7)years, in the NAFLD group was found to be similar to that of Bhatt KN et al.[6] In our study more male prevalence (58.3%)was seen. like that found by Salgado Junior W et al.[7] ,Arun J et al.[8] and Kalra et al.[9] . But some studies [10,11] reported more prevalence of NAFLD in female diabetics. Fasting blood sugar value was approx. to that found by Bhakhtar et al.[5].In our study, mean HbA1c was significantly higher (7.94± 2.12) in NAFLD patients in comparison to non NAFLD (6.61± 0.59). A few studies[12,13,14] show similar results. Whereas some suggested a non significant association of HbA1c with NAFLD in T_2DM[15,16].

In our study, lipid parameters show significant values like that by Patel et al(2018)[14], Vishwanathan et al.(2010)[13], Chandel K et al.(2016)[17] and Somalwar AM et al.(2014)[18].Chaudhary et. al (2020)[12] found similar significant higher values of Tot. cholesterol and TG. Mohan V et. al(2008) suggested significant higher value of Total cholesterol and significantly lower value of HDL[19].

Transaminases levels were statistically non significant between the groups (p=0.38,0.63 for ALT and AST resp.). Bhatt et al. also found similar non significant values[6]. However, Reid AE[10]. show mild to moderate elevations.

In this study approx.30% of NAFLD patients had CAD. Vishwanathan et al.(2010)[13] reported similar result. Others [16,18] found significant association between NAFLD and CAD.

Few studies[20,21] have shown a well established association between fatty liver, impaired glucose tolerance, diabetes mellitus and dyslipidemia. Increased BMI and intra abdominal fat can cause insulin resistance. Thus, the insulin deficiency caused leads to massive lipolysis, mobilising higher FFA to liver, where Triglycerides synthesis increases. This ultimately leads to fat accumulation[22]. Our study shows a positive correlation between BMI and Triglyceride level.

In NAFLD, cause of CAD has been presumed to be the increased production of pro-inflammatory markers such as uric acid and CRP[23], IL-6, TNF-α and profibrogenic markers such as tumor growth factor-β, endothelin 1 and insulin like growth factor-1[24]. The RISC (Relationship between Insulin Sensitivity and Cardiovascular disease) study has shown an increased 10 year CAD risk score in NAFLD diabetics [25] .

However, our study has got few limitations. Ultrasonography was the sole investigation for diagnosis of NAFLD, and not confirmed by liver biopsy. But liver biopsy cannot be applied to large epidemiological studies. Conversaly, ultrasonography stays the commonest way of diagnosing NAFL in clinical practice with sensitivity and specificity of 80% 99% resp. [26,27].

CONCLUSION

NAFLD is associated with several cardiometabolic risk factors for CAD. So, we should perform early screening of type 2 Diabetes for NAFLD. If found, should be managed aggresively so as to minimise the risk of CAD.

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