 DOI: 10.18231/2348-7682.2016.0008

# A study of prevalence of non-alcoholic fatty liver disease in type 2 Diabetes Mellitus

**Kuldeep Chandel[1,*], Sandeep Kumar[2], Waseem Farooqui[3], Mahak Lamba[4]**

[1]Assistant Professor, [2,3,4]Junior Resident, Dept. of Medicine,
MLB Medicine College, Jhansi

***Corresponding Author:**
Email: kuldeepchandel@rediffmail.com

## Abstract

Nonalcoholic fatty liver disease (NAFLD) is one of the common causes of chronic liver disease worldwide and is an emerging important cause of liver disease in India. In the general Indian population, the prevalence of NAFLD is approximately 9- 30% but much higher estimates are reported in obese and patients with type 2 diabetes mellitus. Total of 185 diabetic and 105 non-diabetic patients were randomly selected from diabetic and medicine OPD. After taking informed consent, all patients undergone history, examination and routine laboratory investigations, LFT, lipid profile, HbA1c, serum ferritin, C-reactive protein and USG. The results of cases and control were compared with unpaired t -test and p value <.05 was considered significant. The study group (n=185) was divided into a NAFLD group (n=102) and a non-NAFLD group (n=83) and non-diabetic control (n=105). The prevalence of NAFLD in DM was 55.68% and in non-diabetic was 20%. The NAFLD was significantly associated with high BMI, waist circumference and waist hip ratio, higher HbA1c, higher triglyceride levels, hypercholesterolemia, low HDL levels. Serum CRP level ($p<0.00001$) and serum ferritin level ($p<0.0001$) were significantly high in NAFLD patients with DM-2. This study showed that patients with central obesity, Poor Glycemic control and dyslipidemia are at increased risk of developing NAFLD. Serum ferritin and Serum CRP could be good noninvasive marker for screening of NAFLD in asymptomatic patients.

**Keywords**: Nonalcoholic fatty liver disease, Ferritin, Diabetes mellitus.

## Introduction

The prevalence of diabetes is increasing world over and is expected to affect 57 million adults in India by 2025.(1) Nonalcoholic fatty liver disease (NAFLD) is today considered the most common cause of chronic liver disease and abnormal liver enzymes in both adults and children in both the developed as well as developing countries.(2)NAFLD is characterized by excessive fat accumulation in the liver parenchyma of patients who have no history of alcohol abuse (<20 g per day in men and <10 g in women) in the absence of other identifiable causes of fat accumulation, such as viral hepatitis, autoimmune hepatitis, alpha-1 antitrypsin deficiency, medications like corticosteroids and ATT. Non-alcoholic fatty liver disease (NAFLD) is linked to metabolic syndrome, and is known to be associated with impaired fasting glycemia and diabetes mellitus. Thus, patients with diabetes have a high prevalence of liver disease and patients with liver disease have a high prevalence of diabetes. Virtually the entire spectrum of liver disease is seen in patients with type 2 diabetes. This includes abnormal liver enzymes, nonalcoholic fatty liver disease (NAFLD), cirrhosis, hepatocellular carcinoma, and acute liver failure. NASH is frequently seen in conjunction with other components of the metabolic syndrome (hypertension, diabetes mellitus, elevated lipids, and obesity).(3) Diagnosis of NAFLD can be made by imaging such as ultrasonography, MRI, CT. Many studies are going on to validate the CRP and Serum ferritin as a diagnostic marker of NAFLD. The prevalence of NAFLD in type 2 diabetes mellitus has not been well studied in India. The present study was undertaken to study the incidence and general characteristics of NAFLD in type 2 DMand use of CRP and serum ferritin as biomarker for diagnosis of NAFLD.

## Material and Methods

This case control study was conducted on randomly selected patients with type 2 diabetes mellitus attending the OPD of Department of Medicine, MLB Medical College, Jhansi over a period of 2 years (2013-2015). Total of 185 diabetic and 105 non-diabetic patients were studied. After taking informed consent from all patients a thorough medical history and physical examination was performed for each patient, including BMI, waist/hip ratio, overnight fasting serum samples were obtained from all the participating patients and fasting blood glucose(FBS), post prandial blood sugar(PPBS), HbA1c, serum ferritin, CRP, LFT, serum lipid profile and all the routine investigation were done. All the patients with type 2 Diabetes Mellitus with age of more than 30 years were included in the study. Patients of chronic liver disease, chronic kidney disease, anemia or with history of taking alcohol or any hepatotoxic drugs were excluded from study.

They were further subdivided into 3 groups on the basis of presence of nonalcoholic fatty liver disease by USG.

**Group A:** DM type-2 with NAFLD(N=103),
**Group B:** DM type-2 without NAFLD(N=82),
**Group C**: Non-diabetic(CONTROLS): (N=105).

All data were analyzed on computer using SPSS version 11.5. Continuous variables are presented as mean ± standard deviation (SD), for association, unpaired t-test was applied and p value <0.05 was considered statistically significant.

## Results

In the present study, total 185 patients of type 2 diabetes mellitus and 105 healthy control of age group between 30 – 70 years were evaluated. The mean age in the study was 52.50±11.69 in Group A, 48.55±10.79 in Group B and 49.17±9.80 in Group C. In our study 103(55.68%) patients among type 2 DM and 21(20%) patient among control group were found to have fatty liver on USG.56% of diabetic male were found to have NAFLD and 55.29%of diabetic female have NAFLD which was not statistically significant(Table 1).

**Table 1 Comparison of study and control group according to USG finding**

| USG | DM (n=185) | | | | Control (n=105) | | | |
|---|---|---|---|---|---|---|---|---|
| | M | F | Total | % | M | F | Total | % |
| Fatty Liver | 56 | 47 | 103 | 55.68 | 11 | 10 | 21 | 20.0 |
| WNL | 44 | 38 | 82 | 44.32 | 49 | 35 | 84 | 80.00 |
| Total | 100 | 85 | 185 | 100% | 60 | 45 | 105 | 100% |

We observed that raised level of FBS, PPBS, $HbA_1c$ levels, were significantly (p value 0.0001) associated with NAFLD in diabetic patient. In our study increased waist hip ratio among male (p value 0.0001) and female (p value 0.0001) was significantly associated with NAFLD in DM-2. We observed that increased BMI >25 $kg/m^2$was significantly associated (p value< 0.0001) with NAFLD in DM-2 patient. We observed that serum AST, ALT, GGT and AST/ALT <1 ratio were significantly high among NAFLD with type 2 DM patients. There was statistically significant association between high serum total cholesterol, high serum triglyceride, and low HDL levels and no significant association was seen with LDL, VLDL in patient of NAFLD with DM-2(Table 2).

**Table 2: Comparison of various characteristics in study and control group**

| Parameter | Case (mean±SD) | DM without NAFLD (mean±SD) | Control (mean±SD) | P value b/w group A and B | P value b/w group A and C |
|---|---|---|---|---|---|
| FBS (mg%) | 177±62.8 | 141.4±38.5 | 96±10.5 | .0001 | .0001 |
| PPBS(mg%) | 262.6±67.5 | 214.8±72.8 | 128±16.2 | .0001 | .0001 |
| $HbA_1c$) %) | 9.2±3.4 | 7.6±2.8 | 5.2±1.5 | .0007 | .0001 |
| WHR Female | .85±0.04 | 0.81±0.09 | 0.81±0.08 | .0001 | .0001 |
| WHR Male | 0.89±0.09 | 0.86±0.06 | 0.85±0.05 | .01 | .0001 |
| BMI (kg/m2) | 29±3.62 | 26±3.5 | 24±2.66 | .0001 | .0001 |
| ALT (IU/L) | 57.22±26.3 | 38.6±19.4 | 27.6±18.1 | .0001 | .0001 |
| AST (IU/L) | 37.45±16.3 | 22.36±14.6 | 24.6±16.1 | .0001 | .0001 |
| AST/ALT | .87±.24 | .98±.14 | .92±.11 | .0001 | .0001 |
| GGT (IU/L) | 49.45±14.63 | 26.15±16.7 | 21.62±12.7 | .0001 | .0001 |
| ALP (IU/L) | 112.45±76.3 | 107.25±66.4 | 108.12±56.8 | .62 | .64 |
| S.BIL (mg%) | 1.02±.32 | .98±.18 | .98±.17 | .09 | .06 |
| TC (mg/dl) | 216.5±40.44 | 183.6±35.4 | 176.6±33.1 | <.0001 | .0001 |
| HDL(mg/dl) | 38.3±3.3 | 41.36±4.6 | 42.2±4.71 | .0001 | .0001 |
| TG(mg/dl) | 179.8±67.24 | 137.98±32.14 | 135.2±30.71 | .0001 | .0001 |
| LDL(mg/dl) | 139.45±34.63 | 132.15±28.7 | 131.44±27.4 | .12 | .06 |
| VLDL(mg/dl) | 39.45±16.3 | 33.25±15.4 | 32.12±14.8 | .07 | .12 |

In our study the mean duration of DM in NAFLD group was 10.3 years and in non NAFLD group was 6.6 years, which was statistically significant with p value<.001.For the evaluation of serum CRP comparison between group A and C: P<0.00001, comparison between group A and B, P <0.00001, we observed that increased serum CRP level was significantly associated with NAFLD in DM-2 patients. The Serum ferritin normal range was considered 50-150 ng/ml. Comparison between group A and group B (P<0.0001), comparison between group A and group C (p<0.0001). We observed that increased serum ferritin level was significantly associated with NAFLD in DM-2 patient(Table 3).

**Table 3: Comparison of study and control group on the basis of duration of diabetes mellitus, serum CRP levels and serum ferritin levels**

| **Duration of DM(in yrs)** | **DM with NAFLD (n=103)** | | **DM without NAFLD (n=82)** | | | |
|---|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | | |
| <5 | 17 | 16.50 | 51 | 62.19 | | |
| 5-10 | 36 | 34.95 | 21 | 25.60 | | |
| >10 | 50 | 48.54 | 10 | 12.19 | | |
| Mean±SD | 10.3±6.7 | | 6.6±5.3 | | | |
| P value | <0.001 | | <0.009 | | | |
| **Serum C-reactive protein** | **DM with NAFLD (n=103) A** | | **DM without NAFLD(n=82) B** | | **Control (n=105) C** | |
| | **No.** | **%** | **No.** | **%** | **No.** | **%** |
| Positive(>6mg/dL) | 68 | 66.02 | 13 | 15.8 | 8 | 7.62 |
| Negative<6mg/dL | 35 | 33.98 | 69 | 84.14 | 97 | 92.38 |
| **Serum Ferritin** | **DM with NAFLD (n=103) A** | | **DM without NAFLD(n=82) B** | | **Control (n=105) C** | |
| | **No.** | **%** | **No.** | **%** | **No.** | **%** |
| >ULN(>150 ng/ml) | 70 | 67.96 | 18 | 21.9 | 17 | 16.19 |
| Normal range (50-150 ng/ml) | 33 | 32.04 | 64 | 78.1 | 88 | 84.0 |
| mean±SD) | 246.7±89.26 | | 141.2±49.6 | 138.6±32.10 | | |

## Discussion

NAFLD is strongly associated with overweight/obesity and insulin resistance. The risk for advanced liver fibrosis is highest in individuals with NASH who are older than 40 – 45 yrs of age and overweight/obese or afflicted with T2 DM. This relationship among T2DM, insulin resistance (IR) and NAFLD is expected because insulin is subsequently delivered directly to the portal vein after secretion, taking the same route as the absorbed glucose, and the liver eliminates a large portion of portal insulin at the first pass. In our study we observed that prevalence of NAFLD in diabetes was 55.68% and in healthy control was 20%. This was comparable to Arun J et al[4](56.5%) and S Kalra et al[5] (56.5%) diabetes mellitus patients were identified as having NAFLD. Increased duration of diabetes was significantly associated with NAFLD. Mean duration of DM in NAFLD group was 10.3year and in non NAFLD group was 6.6year in another study by Viswanathan et al.[6]

Our study suggests that as glycaemic control worsens the risk of developing NAFLD increases. In our study we found that raised values of FBS, PPBS and HbA1c correlated significantly with the incidence of NAFLD, with p-values being, 0.006, <0.001, 0.001 respectively. These findings was also seen in other studies like, Giorgio Bedogni et al[7](p value 0.007) and also in Giovanni et al[6] (p value<0.0001). In DM -2 patient with NAFLD serum AST was >ULN in 33.9%, ALT in 36.8%, GGT in 27.1%, ALP IN 38%, serum bilirubin (>2mg%) in 16% patients. Jayarama N et al[8] observed that the mean level of ALT in the cases and controls was 66.68 IU/L and 32.58 IU/L respectively, which was statistically significant. Salmela et al[9] found that the prevalence of elevated ALT levels among the type 2 DM patients was 22.9%.

Obesity in NAFLD is associated with dysfunctional adipose tissue and lipotoxicity promotes insulin resistance and pancreatic β-cell dysfunction. Mean BMI in our study among DM with NAFLD group was(29+3.62) kg/m2,in DM without NAFLD was(26+3.5) kg/m2, this was comparable to study by Vishwanath et al,[6] they observed that mean BMI in among DM with NAFLD group was(29.7+7) *kg*/m2,in DM without NAFLD group was(26.4+4) *kg*/m$^2$. A statistically significant relation was found with the incidence of NAFLD and high waist hip ratio and raised waist circumference with a p-value of <0.001. This correlation was also found in studies like AK Agarwal et al (10)(p-value 0.033) and Giorgio Bedogni et al[7] (p value 0.001). In our study dyslipidemia was found to be a strong risk factor for NAFLD. Hypercholesterolemia(67.9%),hypertriglyceridemia(63.1%), and low HDL(66%) were significantly associated and no significant association was seen with LDL and VLDL in patient of NAFLD with DM-2. MV Jalil et al[11] found that Hypercholesterlemia- 52%, Hypertriglycerdemia- 67%, High LDL- 59% and Low HDL- 27%) were significantly higher among subjects with NAFLD-Group. In a hospital based study from North India Prashanth et al[12] found almost similar findings.

Over time, several biological markers have been studied for evaluating the extent of steatosis, the presence of necro-inflammation, and the development of fibrosis to avoid performing liver biopsy, an invasive

procedure that still represents the gold standard of diagnosis. The two which have been extensively linked are C reactive protein and serum ferritin. In our study serum C-reactive protein (CRP) was high in diabetes with NAFLD group in (66%) patients with similar observation were made by Kuangchunhu et al[13] shows that Serum CRP levels were significantly higher in patients with hepatosteatosis than in healthy control. A SF >1.5 × ULN is associated with hepatic iron deposition, a diagnosis of NASH, and worsened histologic activity and is an independent predictor of advanced hepatic fibrosis among patients with NAFLD.[14] Furthermore, elevated SF is independently associated with higher NAS, even among patients without hepatic iron deposition. In our study Serum Ferritin was found significantly high in diabetic with NAFLD group in 67.9% cases with mean (246.7±89.26)ng/mL with p value <.0001.Similar observation was made by T J Hsaiaoet al[15] also observed that serum ferritin was significantly higher in NAFLD than control group (113.86±99.59ng/mL vs 38±36.7ng/mL).

Our study is well in concordance with the above studies in showing an association between diabetes mellitus and NAFLD. The study also emphasizes on the association between obesity, duration of diabetes mellitus and poor glycemic control with NAFLD. Serum CRP and Serum Ferritin levels are also consistent non-invasive markers and result of which was in agreement to the above mentioned studies.

## Conclusion

Patients with type II diabetes mellitus are at increased risk for developing NAFLD when compared to general population. The risk is further intensified in patients having obesity, poor glycemic control and dyslipidemia. Serum CRP and Serum CRP levels were significantly high among NAFLD patients, thus holding a propitious role as a non – invasive marker for diagnosis of NAFLD. Patients with established type 2 diabetes mellitus should be screened for NAFLD to avoid diabetes worsening and associated chronic complication which can be ameliorated with early clinical intervention.

## References


1. Pradeepa R, Deepa R, Mohan V. Epidemiology of diabetes in India--current perspective and future projections. J Indian Med Assoc2002 Mar;100(3):144-8.
2. Angulo P, Lindor KD. Non-alcoholic fatty liver disease. J GastroenterolHepatol2002; 17 (Suppl):S186–S190.
3. Hsiao PJ, Kuo KK, Shin SJ. Significant correlations between severe fatty liver and risk factors for metabolic syndrome. J Gastroenterol Hepatol2007;22:2118–2123.
4. Arun J, Clements RH, Lazenby AJ, Leeth RR, Abrams GA. The prevalence of nonalcoholic steatohepatitis is greater in morbidly obese men compared to women. Obes Surg 2006 Oct;16(10):1351-8.
5. Kalra S, Vithalani M, Gulati G, Kulkarni CM, Kadam Y, Pallivathukkal J, et al. Study of prevalence of non-alcoholic fatty liver disease(NAFLD) in type 2 diabetes patients in India (SPRINT).J Assoc Physicians India 2013 Jul;61(7):448-53.
6. V Viswanathan, Mahesh Kadiri, Srikanth Medimpudi, Satyavani Kumpatla. Association of NAFLD with diabetic micro and macrovascular complications in South Indian diabetic subjects. International J of Diabetes in Developing Countries 2010;30(4):208.
7. Bedogni G, Miglioli L, Masutti F. Prevalence of and risk factors for nonalcoholic fatty liver disease: the Dionysos Nutrition and Liver Study. Hepatology 2005;42:44–52.
8. Aparna G, Prabhakar K, Jayaram N, Raghavendra Prasad BN. Prevalence of autoimmune markers in young adults with diabetes. Diabetes - Journal of the Association of Physicians of India Feb2014;62.
9. Salmela PI, Sotaneimi EA, Niemi M. Liver Function test in diabetic patients. Diabetic care 1984;7:248.
10. AK Agarwal, V Jain, S Singla, BP Baruah, V Arya. Prevalence of non-alcoholic fatty liver disease and its correlation with coronary risk factors in patients with type 2diabetes. JAPI 2011 Jun;59:351-4.
11. MV Jali, Sanjay Kambar, Sujata M. Jali, Murigendra B. Hiremath. Prevalence of non- alcoholic fatty liver disease among type-2 diabetes mellitus patients – A cross-sectional hospital based study. Al Ameen J Med Sci 2015;8(1):50-54.
12. Prashanth M, Ganesh HK, Vima MV, John M, Bandgar T, Joshi SR, et al. Prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus. Assoc Physicians India 2009 Mar;57:205-209.
13. KCHu, HY Wang, SC Liu, CC Liu. Nonalcoholic fatty liver disease: Updates in noninvasive diagnosis and correlation with cardiovascular disease - World Journal of Gastroenterol 2014 Jun 28;20(24):7718-29.
14. Kowdley KV, Belt P, Wilson LA, Yeh MM, Neuschwander-Tetri BA, Chalasani N, et al. Serum ferritin is an independent predictor of histological severity and advanced fibrosis in patients with non-alcoholic fatty liver disease. Hepatology2012 Jan;55(1):77-85.
15. Hsiao TJ, Chen JC, Wang JD. Insulin resistance and ferritin as major determinants of non-alcoholic fatty liver disease in apparently healthy obese patients. Int J ObesRelatMetabDisord2004 Jan;28(1):167-72.