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Prevalence of NAFLD in Type-2 Diabetic Patients in Rural Population of Muzaffarnagar Region

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Abstract: ***Background: Non-alcoholic fatty liver disease (NAFLD) is commonly associated with type 2 diabetes mellitus (DM). We carried out a prospective case-control study showing correlation of NAFLD in patients with type 2 DM and its connection with Insulin Resistance. Materials and Methods: Total 97 patient out of 100 patients of Type – 2DM attending Muzaffarnagar medical college and hospital completed the study and were evaluated using SPSS software version 12. Abdominal ultrasound was performed to establish the presence of fatty liver. For assessment of Insulin Resistance, Homeostasis Model Assistant - Insulin Resistance (HOMA-IR) was calculated. A probability value of P < 0.05 was considered statistically significant. Results: The study group of 100 was divided into a NAFLD group of 45 and a non-NAFLD group of 55 with NAFLD as 45%. The NAFLD subgroup had excessive obesity which was measured by BMI and central obesity was measured by waist circumference and waist hip ratio, higher HbA1c and higher triglyceride levels. HOMA-IR for Insulin Resistance was significantly higher in NAFLD group than Non NAFLD group (P value 0.03). Conclusion: The frequency of NAFLD is high in patients of Type 2 DM. Insulin resistance correspond with the presence of NAFLD among T2DM patients.***

Keywords: Insulin Resistance, non-alcoholic fatty liver disease, type 2 diabetes mellitus

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) denotes a wide range of conditions occurring in those who do not consume alcohol in amounts, generally considered to be harmful to the liver and distinguished histologically by macrovascular hepatic steatosis. NAFLD is the hepatic pandemic of the twenty-first century, being the prime cause of chronic hepatic disease in the world. [1] It is emerging as the most popular chronic liver disease in both Western countries and also in other parts of the world. [2, 3] NAFLD is a diseaseof our generation which has burst onto the clinical landscape over the past 25 years. The problem of NAFLD is not restricted to its potential to cause serious liver-related morbidity and mortality. It often occurs with features of the metabolic syndrome including obesity, type 2 diabetes mellitus [4, 5], Dyslipidemia [6] and hypertension [8]. No wonder 10–75% of NAFLD patients have T2DM and 21–72% of patients with diabetes are reported to have NAFLD [8].

NAFLD has been connected very closely with the presence of type 2 diabetes mellitus. DM is an important decisive factor of both presence and severity of NAFLD. Insulin resistance plays a central role in the pathogenesis of NAFLD although the initial site and root of insulin resistance is unknown. The two key pathophysiologic abnormalities associated with insulin resistance that play a role in the genesis of a fatty liver are hyperinsulinemia and increased free fatty acid delivery to the liver. [9] The mortality rate of diabetic patients due to cirrhosis is more than twice the general population and patients with both NAFLD and DM have a poorer prognosis in terms of higher rates of cirrhosis and mortality. [10] Available literature on NAFLD and its relation to coronary artery disease in diabetes patients from India is very Less. This may be related to the assumption that the condition is benign and has a nonprogressive course. In addition, a large burden of viral hepatitis in India tends to reduce the concern accorded to this condition. Hence, the present study was planned to study of NAFLD in type 2 Diabetes mellitus patients in Muzaffarnagar medical college and hospital and its correlation with Insulin Resistance.

2. Material and Method

The present study was carried out at Muzaffarnagar medical college and hospital and Biochemistry Department from January 2019 to October 2019. Initial screening in the form of detailed history taking and clinical examination was carried out to include/exclude the patients in the study. A total 100 patients with age more than 20 years were included who were having diabetes of minimum 2-year duration. Exclusion criteria included: patients who consumed more than 50 g alcohol per week, patients who were found to have other liver diseases such as malignancies, hepatitis, liver abscesses, and patients having derangement of hepatic functions due to any other febrile illnesses/disease. A detailed history regarding the disease was taken, and complete physical examination was done. Obesity was calculated by BMI, whereas waist/hip ratio was measured as an index of fat accumulation. [11, 12]. Serum samples after overnight fasting were obtained from all subjects for liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and alkaline phosphates), serum lipid profile (total cholesterol, triglycerides, high-density lipoprotein cholesterol [HDL-C], and low-density lipoprotein cholesterol [LDL-C]), fasting blood glucose (FBS), HBA1C, and fasting insulin levels. Homeostasis Model Assistant–Insulin Resistance (HOMA-IR) was calculated as measures of insulin resistance and sensitivity using following formula:

HOMA-IR= [fasting insulin (μU/ml) ×fasting glucose (mmol/l)]/22.5.

Abdominal ultrasonography was done on all subjects.

Statistical analysis was done by SPSS Version 16. All results are presented as Mean±S.D. A p value of less than 0.05 considered significant.

3. Results

100 patients with type 2 diabetes mellitus were registered during the study period. The mean age of the patient was 55years. Out of 100 patients, 49 were males and 51 were females. None of the patients had histories of alcohol consumption. Of 100 patients with T2DM, 45 were found to have NAFLD in abdominal ultrasonography examination. Prevalence of fatty liver disease was almost same in males and females (23 males and 22 females).

ALT and ASTwas statistically not significant. A large proportion of the study population was obese as mean BMI was 27.09 (17.2–37.05). Table 1 indicate baseline clinical and biomedical parameters of the study population. Both NAFLD and non-NAFLD groups were equated in regard to demographic, anthropometric, and biomedical characteristics. BMI, waist/hip ratio, S. triglyceride level were notably high [Table 2] in NAFLD group as compared to non-NAFLD group (P = 0.009, 0.0001, 0.003, respectively). Computable measures of insulin resistance S. fasting insulin, HOMA-IR score, showed significant association of NAFLD with increased insulin resistance. Other parameters were not differed significantly between the two groups.

4. Discussion

The preponderance of NAFLD in 100 patients of Type 2 diabetes mellitus in the present study was based on abdominal ultrasound examination. Many studies have reported NAFLD among DM patients at approximately 50% [8].No significant changes were therein sex distribution between the two groups. Glycemic control both in terms of fasting glucose as well as HBA1C in patients with NAFLD were not expected as compared to non-NAFLD. (P = 0.07 and 0.24, respectively). This observation indicates a noncausative relationship between glycemic control and fatty liver.

BMI was elevated in patients with NAFLD as compared to Non-NAFLD. The waist/hip ratio was elevated in patients with NAFLD as compared to Non-NAFLD and statistically significant (P = 0.0001). Waist/hip ratio depictsabdominal fat dispersal. Kral et al. observed notable connection between waist/hip ratio and the hepatic steatosis, in patients with normal BMI. [18] Focalisation of Insulin Resistance represents deposits of adiposity with visceral fat and fatty liver and be part of central adiposity. [19] Depot of fat on a organ is a strong call of hyperinsulinemia. Large intra-myocellular triglyceride content as depicted via muscle biopsy is analogous to fat in liver [20] or MRI/computed tomography, [21] closely correspond with muscle IR. Deranged accumulation in a sequence of events of triglycerides is the overflow hypothesis, [22] according to which IR is the result of the incapability of the adipose organ tofit in with excess calories. As the extent of the fat cell to store triglycerides is out done, fat spills to other tissues (muscle and liver), where the intracellular triglyceride metabolism impede with insulin signalling, glucose transport/phosphorylation, and glycogen synthesis in muscle and rises hepatic gluconeogenesis.

In this study, we noticed that patients in the NAFLD group had a higher preponderance of Insulin resistance as measured by S. fasting insulin, HOMA-IR, as compared to non-NAFLD group (P − 0.03 and 0.04, respectively). In insulin-resistant states, hyperinsulinemia may increase membrane-bound transcription factor SREBP-1c, which switch on most genes involved in lipogenesis. Hyperinsulinemia may trigger hepatic fat deposition, as indicated by the hepatic steatosis occurring under the capsule of livers in patients on peritoneal dialysis, [23] where insulin added to the dialysate. This information suggest a primary role of dysfunctional lipid metabolism in the beginning and perseverance of NAFLD, and hence lipotoxicity, [24] leading to ectopic lipid accumulation. The strongest evidence of IR in the pathophysiology of NAFLD is designed to improve insulin sensitivity in the liver [25-28] (Metfromin) and the periphery [29]. Mean cholesterol, HDL, and LDL levels did not hinder much between the two groups. Only the mean triglyceride levels showed significant preponderance with the presence of NAFLD (P = 0.03). Dyslipidemia are related with NAFLD. Studies have shown that 21–93% of patients diagnosed with NAFLD have hyperlipidemia, [8] including hypertriglyceridemia, hypercholesterolemia or both. [14] Almost 50% of the patients diagnosed with hyperlipidemia had NAFLD on ultrasound evaluations but only hypertriglyceridemia was a risk of developing liver fatty disease. [30] Hypertriglyceridemia with diabetes and obesity rises the risk of NAFLD development. [31] Transaminase levels were not significant between the NAFLD and non-NAFLD groups (P = 0.06 and 0.05 for AST and ALT, respectively). Mild to moderate elevations of serum aminotransferase are common in NAFLD, [14] and normal values can be found in up to 78% of patients at any time, even when complete histological findings are present. [32] Depicting a poor correlation between transaminase levels and disease. [14] The clinical spectrum of NAFLD wants research to determine its pathogenesis and to improvise diagnostic modalities. Improved imaging techniques and the discovery of serum biomarkers, will enable a more accurate diagnosis of NASH without a liver biopsy. A multimodal treatment plan is the best option. [33] A limitation of this study is that the diagnosis of NAFLD was based on ultrasonography and was not confirmed by liver biopsy. Radiological features cannot distinguish between steatohepatitis and other types of NAFLD, and that only liver biopsy can assess the severity of damage and the prognosis. [8, 32] Liver biopsy is not applied in large epidemiological studies. Conversely, ultrasonography is the most common method of diagnosing NAFLD in clinical practice and has a very good sensitivity and specificity in detecting moderate and severe steatosis in patients with the biopsy-proven disease. [8, 32, 34] Indeed, it has been reported that the presence of >33% fat on liver biopsy is optimal for ultrasound detection of steatosis, although ultrasonography is not completely

sensitive, particularly when hepatic fat infiltration is <33%. [35]

Table 1

DEMOGRAPHIC, ANTHROMETRIC, AND BIOMEDICAL CHARACTERISTICS OF 100 PATIENTS WITH TYPE 2 DM
PARAMETER MEAN RANGE SD
AGE(YEARS) 54 20-80 13.40
BMI(KG/m2) 26 17-36.02 4.01
Waist hip ratio 0.79 0.78 -1.0 0.075
ALT(IU/L) 14.89 1-71 13.15
AST(IU/L)16.0 1-92 13.0
LDL(mg/dl) 114.4 24-189 35.4
TRIGLYCERIDE(mg/dl) 182.0 53-389 55.0
CHOLESTROL(mg/dl)189.5 69-272 38.0
INSULIN(µU/dl) 14.4 3-69 8.6
HbA1c(%) 7.5 5.8-12.5 1.2
FBS(mg%) 114.4 67-318 33.5
HOMA-IR 4.5 0.7- 43.4 4.8
Comparison parameters between NAFLD and Non -NAFLD diabetic patients
Parameter NAFLD Non NAFLD p
Age(yr) 55.92(±12.96) 52.53(13.7) 0.2
BMI(kg/m2) 27.26(3.76) 25.18(4.01) 0.008
Waist hip ratio 0.89(0.05) 0.82(0.06) 0.001
FBS(mg/dl) 121.0(41.7) 108(24.01) 0.06
HbA1c% 8.0(1.38) 7.79(1.17) 0.23
HOMA-IR 5.20(6.78) 3.2(1.98) 0.02
Insulin(µU/dl) 16.95(11.12) 13.62(5.64) 0.02
HDL(mg/dl) 39.02(7.01) 13.41(6.65) 0.7
LDL(mg/dl) 119.05(37.2) 111.12(33.63) 0.2
Cholestrol 194.07(36.8) 185.8(39.02) 0.2
Triglyceride 200.4(63.3) 167.4(42.61) 0.003 (mg/dl)
AST(IU/L) 17.63(15.59) 12.68(9.63) 0.06
ALT(IU/L) 18.7(15.85) 13.96(10.07) 0.05

5. Conclusion

The present study reported a high incidence of NAFLD in Type 2 diabetes patients emphasizing the need for early screening. Our findings support the hypothesis that Insulin resistance was associated with the presence of NAFLD among diabetic patients. Follow-up studies using larger cohorts of patients are necessary to confirm these results and to broaden these findings among NAFLD patients without type 2 diabetes

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