

Incidence of nonalcoholic fatty liver disease in patients undergoing laparoscopic cholecystectomy

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ABSTRACT

Introduction: Nonalcoholic fatty liver disease (NAFLD) includes a host of disease spectrum ranging from simple steatosis to steatohepatitis, cirrhosis liver, and even hepatocellular carcinoma. NAFLD can occur at all ages, and the highest prevalence is found in the age group of 35–55 years. NAFLD is becoming the commonest cause leading to hepatic cirrhosis, but there is no prescribed therapy for this common condition. Reduction in body weight may reverse the condition. **Aim:** To find the prevalence of NAFLD in a cohort of patients undergoing laparoscopic cholecystectomy in this part of the country and also to evaluate the usefulness of routine liver biopsy for the diagnosis of NAFLD. **Materials and Methods:** Interventional type of cross-sectional study. In all, 200 consecutive patients underwent a liver biopsy at the end of a standard laparoscopic cholecystectomy, and detailed histopathological examination was done. Clinical, biochemical, demographic, and anthropometric variables were obtained prospectively. NAFLD Activity Score (NAS) was obtained for each patient. Statistical analysis was done using SPSS version 22. **Results:** A total of 200 patients (140 females and 60 males) were included in the study. In all, 138 patients were categorized as non-non-alcoholic steatohepatitis (NASH), 39 patients as borderline/suspicious NASH, and 23 patients had definitive NASH. A higher body mass index, weight, total cholesterol, low-density lipoprotein, alkaline phosphatase, and weight circumference were found in patients with NASH. **Conclusion:** The high prevalence of NAFLD in patients with gallstone disease may justify routine liver biopsy during cholecystectomy to establish the diagnosis, stage, and possibly direct therapy.

Keywords: Gallstone disease, liver biopsy, obesity, steatohepatitis

Introduction

Nonalcoholic fatty liver disease (NAFLD) is emerging as the most common liver abnormality affecting 2.8%–24% of the general population worldwide.^[1] NAFLD ranges from fatty liver to steatohepatitis without significant liver damage to hepatocellular inflammation and damage with or without significant fibrosis and cirrhosis in the absence of significant alcohol intake.^[2–4] NAFLD usually occurs in two phases. Initially, triglycerides are deposited in the hepatocytes without causing any damage to the liver. But later on due to lipid peroxidation and oxidative stress, hepatic damage takes place.^[5,6] Patients with gallstones are found to have associated NAFLD as both the disease conditions

share similar risk factors such as obesity, diabetes mellitus, and hypertriglyceridemia.^[7]

Materials and Methods

The study was conducted from September 2015 to August 2017. Consenting patients above 18 years of age with no history of alcohol intake for the past 6 months and seronegative for hepatitis B and C were included in the study.

Keeping the prevalence at 32% by Mohan *et al.*^[8] in South India and by Majumdar *et al.*^[9] at 30.7% in Northern India in community-based studies; the absolute precision was kept at 10%, and the sample size was determined to be 87. By keeping a design effect of two, the sample size was calculated at 174. The final sample size was calculated at 200 keeping the refusal rate at 15%.

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Patients with clinical or biochemical evidence of hepatitis due to autoimmune, viral hepatitis, genetic, cholestatic, or drug-induced etiology and also patients with history of alcohol intake of ≥ 20 g/day were excluded from the study.

At the end of standard laparoscopic cholecystectomy, liver tissue of approximately 1.5 cm in diameter was taken with endo scissor and sent for histopathological examination. The tissues were examined under hematoxylin–eosin stain for morphological features of ballooning, steatosis, and lobular inflammation; and Masson's trichrome stain was used for fibrosis staging.^[10]

Each biopsy specimen was evaluated by NAFLD Activity Score (NAS) proposed by the NASH Clinical Research Network (CRN).^[10] Based on the NAS-CRN, the biopsies were categorised as non-non-alcoholic steatohepatitis (NASH), borderline/suspicious NASH, and definitive NASH. Steatosis was graded as Grade I: $>5\%$ – 33% , Grade II: $>33\%$ – 66% , and Grade III: $>66\%$.^[11,12]

NAS score ranges from 0 to 8 after taking into account the unweighted sum of scores of steatosis (0–3) ballooning (0–2), and lobular inflammation (0–3). A value of NAS <3 was categorised as non-NASH, 3–4 as suspicious/borderline NASH, and >5 as NASH.

Fibrosis was staged on a scale of 0–4 as follows:^[10]

- Stage 0: absence of fibrosis
- Stage 1: perisinusoidal or portal fibrosis (1a: mild/delicate zone 3 fibrosis, 1b: moderate/dense zone 3 fibrosis, 1c: portal fibrosis only)
- Stage 2: peri-sinusoidal and portal/periportal fibrosis
- Stage 3: septal or bridging fibrosis
- Stage 4: cirrhosis

Means with standard deviation of various variables were calculated and their means were compared using independent samples *t*-test.

Results

A total of 200 patients (140 females and 60 males) were included in the study. In all, 138 patients were categorized as non-NASH, 39 patients as borderline/suspicious NASH, and 23 patients had definitive NASH. The mean age in patients with NASH was 39.47 ± 11.701 years, and in non-NASH group the mean age was 38.64 ± 12.124 years.

The other parameters between the two groups are shown in the Table 1. There was no difference in the levels of blood sugar, serum bilirubin, aspartate aminotransferase, alanine aminotransferase (ALT), high-density lipoprotein, and height of the patients in both the groups. Body mass index (BMI) in patients with NASH was significantly higher (26.691 ± 2.155) than non-NASH patients (22.861 ± 1.900) with a *P* value < 0.001 . The mean weight was also significantly higher (66.00 ± 8.343 KG) in NASH than non-NASH group of patients (55.22 ± 5.679) with a *P* value < 0.001 .

Table 1: Different parameters in nonalcoholic steatohepatitis and non–nonalcoholic steatohepatitis group of patients

Parameters	Mean \pm SD in NASH group	Mean \pm SD in non-NASH group	<i>P</i>
Blood sugar (random) (mg/dL)	128.76 \pm 3.758	128.07 \pm 3.943	0.245
Height (cms)	156.95 \pm 7.137	155.43 \pm 5.212	0.134
Bilirubin (mg/dL)	0.782 \pm 0.166	0.774 \pm 0.114	0.679
AST (U/L)	24.40 \pm 1.929	24.60 \pm 2.501	0.580
ALT (U/L)	26.73 \pm 2.457	24.14 \pm 3.093	0.188
BMI (KG/m ²)	26.691 \pm 2.155	22.861 \pm 1.900	<0.001
Weight (KG)	66.00 \pm 8.343	55.22 \pm 5.679	<0.001
ALP (U/L)	68.69 \pm 7.933	66.12 \pm 8.530	<0.05
Total cholesterol (mg/dL)	176.63 \pm 8.286	168.83 \pm 10.759	<0.001
LDL (mg/dL)	90.58 \pm 7.858	85.72 \pm 7.742	<0.001
HDL (mg/dL)	67.18 \pm 7.775	68.12 \pm 9.705	0.500
Waist circumference (cms)	82.11 \pm 5.261	73.38 \pm 3.878	<0.001

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BMI: Body mass index; ALP: Alkaline phosphatase; LDL: Low-density lipoproteins; HDL: High-density lipoprotein; SD: Standard deviation; NASH: Nonalcoholic steatohepatitis, mg/dL: milligram/deciliter, cms: centimeters, U/L: Unit/Liter, KG/m²: Kilogram/square meter

Total cholesterol was also found to be higher in the NASH (176.63 ± 8.286 mg/dL) than those in non-NASH group of patients (168.83 ± 10.759) which was statistically significant (*P* < 0.001). Serum low-density lipoproteins were also significantly higher in NASH (90.58 ± 7.858) than in non-NASH group of patients (85.72 ± 7.742) with a *P* value < 0.001 .

Patients in NASH group had higher waist circumference (82.11 ± 5.261 cms) than non-NASH group of patients (73.38 ± 3.878) which is statistically significant (*P* < 0.001). Among the biochemical parameters, only serum alkaline phosphatase was found to be significantly increased in NASH (68.69 ± 7.933) group of patients.

Discussion

In this study, the prevalence of patients with NAFLD was 31% which was similar to the findings of Mohan *et al.* (32%) in urban South Indian population^[8] and Anindo Majumdar *et al.* (30.7%) in rural North Indian population.^[9] Singh *et al.*^[13] and Bajaj *et al.*^[14] in their hospital-based studies found prevalence of NAFLD to be 24.5% and 32.2%, respectively, similar to this study. Similar prevalence was seen outside India also. Dassanayake *et al.*^[15] found a prevalence of 32.6% in middle-aged population in neighbouring Sri Lanka similar to this study. The prevalence ranged from 23.4% to 46% in some other studies.^[16–20] Whereas Farah A *et al.* in the neighbouring Pakistan found a very high prevalence of 62.5%.^[21]

Lobular inflammation and ballooning along with steatosis are the main features required to diagnose NASH.^[22] Liver biopsy is the gold standard to assess and diagnose these histopathological characteristics and also to predict the prognosis.^[4,23,24]

High BMI was seen in patients with NASH similar to the studies of Farah A *et al.*^[21] Higher waist circumference was found among patients with NASH in this study similar to many previous studies.^[8,9,16,20,21]

A high serum cholesterol level was also found in this study similar to other studies.^[8,14] A high ALT level correlates well with high steatosis and high activity as shown by Rastogi *et al.*,^[25] but it was found to be similar in both groups of patients in this study.

Awareness of this entity among the rural surgeons might enable them to undertake studies by ultrasonography while scanning the abdomen for other pathologies and also to check the liver for any fatty changes either grossly or by biopsy followed by histopathological examination of the biopsies, so that proper dietary advice and exercises may be advised to the patients to prevent further progress of their fatty liver conditions.

Conclusion

Patients with cholelithiasis have a high prevalence of NAFLD, which is 31%. Hence, patients at the time of discharge were advised about lifestyle modifications in the form of regular exercises, diet modifications to ingest balanced diets as advised by the Institute's dieticians, to take seasonal fruits regularly, and so on. Patients were also warned about the possible progress of their liver conditions to cirrhosis and even hepatocellular carcinoma if they do not take proper care of their health.

Limitations of the study

The study population was patients with gallstones who share similar risk factors to develop NAFLD. Therefore, the results may not be representative of the general population of the region. Hence, population-based prospective studies may be undertaken to get the actual incidence of NAFLD in the general population.

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Conflicts of interest

There are no conflicts of interest.

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