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ORIGINAL ARTICLE

Incidence of Non-Alcoholic Fatty Liver Disease and Associated Risk Factors

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ABSTRACT

Objectives: To evaluate the frequency of different risk profiles and associated clinical parameters in patients with nonalcoholic fatty liver disease (NAFLD).

Methodology: This cross-sectional study was conducted at the Gambat Institute Of Medical Sciences,Gambat District, Khairpur, between March 2019 to January 2020. A total of 345 patients participated in the study. Demographics, clinical features, investigations, and causative agents of NAFLD were noted in a document. Patients with raised ALT, fatty liver on imaging, aged between 18-75 years were a part of the study. Exclusion criteria included patients with overconsumption of alcohol, positive HBsAg, positive anti-HCV, and other underlying liver diseases with known origin. Patients' blood samples were also tested for fasting blood sugar, random blood sugar, fasting cholesterol and fasting triglyceride levels.Levels of glucose, triglycerides and cholesterol were measured with an autoanalyzer; Photometer 4010; Beohrnger Mannheim; using the enzymatic-calorimetric methods. All data was analyzed using SPSS version 24.

Results: The mean age of the patient was 48.4 ± 12.2 years and a mean body mass index of 30.2 The mean cholesterol was 199.4 ± 54.3 mg/dl. The majority i.e. > 60 percent were women with only 128 (37.1%) males (Table 1). The body mass index (BMI) was significantly higher in female patients as compared to males ($p<0.001$). The males had a significantly greater frequency of traits for metabolic syndrome as compared to women i.e. 111 (86.7%) vs. 145 (66.8%) ($p=0.02$). Obesity in patients was also significantly associated with female gender. We found a significant relationship of hypercholesterolemia in patients with DMT2 ($p=0.04$). Similarly, the majority of the patients i.e. 55 (47%) with DMT2 also had hypertriglyceridemia ($p=0.002$).

Conclusion: The present study indicated that female gender, obesity, and diabetes mellitus were significantly associated with NAFLD. NAFLD places a significant burden on the healthcare system and is associated with poor quality of life of patients. Metabolic syndrome is another leading association that needs to be explored in further detail. Recognition of high-risk profile patients can help establish early diagnosis and hence treatment plans can be implemented at an early stage of disease.

Keywords: fatty liver, chronic liver disease, non-alcoholic liver disease, NAFLD, obesity, diabetes mellitus, dyslipidemia

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD), clinically a histopathological condition, affects the liver at cellular levels, having similar features to liver diseases caused by alcohol. It is reported in people who drink little to almost no alcohol. It envelops a histological course that ranges from the build-up of fat in hepatocytes with no associated inflammation or fibrosis (simple hepatic steatosis) to hepatic steatosis accompanied by necroinflammation (steatohepatitis) that, not necessarily, but may present with fibrosis. This liver condition, nonalcoholic steatohepatitis (NASH), could lead to cirrhosis in approximately 20 percent of patients. NASH is now known to be a leading cause of cryptogenic cirrhosis. [1,2]

Considering the estimation of prevalence, even though noteworthy reviews have demonstrated that almost 24% of the people are reported to have NAFLD in several countries, a more proof-centered approximation is extracted from two data reports from the third National Health and Nutrition Examination Survey (NHANES III) conducted between 1988 and 1994 in the USA.[3] These reports have indicated that 3-6% of the population in the US have some extent of NAFLD diagnosed on the levels of elevated aminotransferases when there is no other existing pathological problem. This diagnostic criterion has been widely accepted by the proof provided by a large histological survey of 354 back-to-back patients with complaints of abnormal liver function tests of unknown origin. Levels of either an alanine transaminase (ALT), a δ-glutamyl transferase or an alkaline phosphatase more than double the upper normal limit for a minimum of 6 months was termed as "abnormal". Two-thirds of the patients had NAFLD, one-third with simple steatosis and one-third with non-alcoholic steatohepatitis (NASH) either with or without fibrosis.[4,5,6]

NAFLD was diagnosed on the basis of clinical histological criteria including absent low alcohol

consumption and a viable liver biopsy demonstrating steatosis, hepatocyte ballooning, apoptosis, Mallory bodies, mixed inflammation associated or not with fibrosis and cirrhosis. NAFLD can also be diagnosed with radiology. All three types of imaging namely ultrasound, CT scan and MRI are sensitive (93-100%) in the identification of a considerably fatty liver.[3] The potential risk factors for NAFLD are reported to be female sex, type 2 diabetes mellitus, obesity, and hyperlipidemia. The frequency of obesity in NAFLD patients ranged between 30 and 100%, of type 2 diabetes ranged between 10 and 75% and of dyslipidemias ranged between 20 and 94%.[3,4] Due to scarcity of local literature the current study was undertaken. The current study focused on assessing the incidence and associated factors in patients with non-alcoholic fatty liver disease (NAFLD).

METHODS AND MATERIALS

This cross-sectional study was conducted at the Gambat Institute Of Medical Sciences,Gambat District, Khairpur, between March 2019 to January 2020 after taking ethical review board approval. Sampling was done adopting the non-probability convenience technique to enroll the participants in the study. A total of 345 patients participated in the study.

Demographics, clinical features, investigations, and causative agents of NAFLD were noted in a document. Before data was collected, patients' informed consent was obtained via signatures. It was made sure that anonymity and confidentiality of the patients would not be violated.

Patients with raised ALT, fatty liver on imaging, aged between 18-75 years were a part of the study. Exclusion criteria included patients with overconsumption of alcohol, positive HBsAg, positive anti-HCV, and other underlying liver diseases with known origin.

Clinically, NAFLD was diagnosed on the basis of elevated ALT in addition to a fatty liver on ultrasound exhibiting the following characteristics; i) a diffuse hyperechoic echotexture (bright liver), ii) increased liver echotexture compared with the kidneys, iii) vascular blurring, iv) deep attenuation. Diagnosis of NAFLD on the basis of histopathology is made by the presence of macrovesicular steatosis in hepatocytes, resulting in the dislocation of the nucleus to the margin of the cell. Moreover, presence of characters like Mallory bodies, ballooning degeneration, predominantly lobular neutrophilic inflammation, and Rappaport zone III perisinusoidal fibrosis were suggestive of presence of fatty liver.

Participants who agreed to biopsy got their blood samples sent for complete blood count, coagulation profile, and biopsy was taken using the tru cut liver biopsy needle under directions provided by ultrasound. The samples were then sent to the department of pathology for proper examination. Patients were also tested for fasting blood sugar, random blood sugar, fasting cholesterol and fasting triglyceride levels. Height was documented in meters and the Body Mass Index (BMI) was calculated using the following formula; BMI = Weight in kilograms/(Height in meters)^2

Levels of glucose, triglycerides and cholesterol were measured with an autoanalyzer; Photometer 4010; Beohrnger Mannheim; using the enzymatic-calorimetric methods. Continuous variables of age, ALT, BMI, fasting triglycerides, fasting and random blood sugar levels were presented as mean and standard deviation. Categorical data was tabulated as percentages included gender and presence or absence of symptoms (like anorexia, dyspepsia, right upper quadrant pain), fatty liver on ultrasound, fatty change on histopathology, obesity, diabetes, hypertension, and hypertriglyceridemia. Data entry and analysis was done using SPSS version 24 software.

RESULTS

The mean age of the patient was 48.4 ± 12.2 years and a mean body mass index of 30.2 The mean cholesterol was 199.4 ± 54.3 mg/dl. The majority i.e. > 60 percent were women with only 128 (37.1%) males (Table 1).

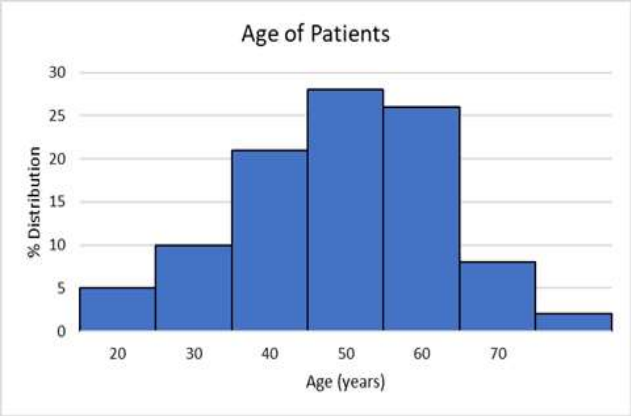

Figure 1. Age Distribution in Patients with NAFLD Discussion

Age distribution is illustrated in figure 1. The majority of the patients were between the ages of 40-50 years.

Table 1. Patient Demographics

	n=345
Age (years)	48.4 ± 12.2
Cholesterol (mg/dL)	199.4 ± 54.3
Triglyceride (mg/dL)	181.2 ± 57.6
BMI (kg/m2)	30.2 ± 5.3
ALT IU/L	83 ± 28.5
Gender	
female	217 (62.9%)
male	128 (37.1%)
Diabetes mellitus	
yes	117 (33.9%)
no	228 (66.1%)
Hypertriglyceridemia	
yes	166 (48.1%)

no	179 (51.9%)
Hypercholesterolemia	
yes	97 (28.1%)
no	248 (71.9%)
Metabolic syndrome	
yes	90 (26.1%)
no	255 (73.9%)
Metabolic syndrome traits	
None	59 (17.1%)
One trait	72 (20.9%)
Two traits	124 (35.9%)
Three traits	62 (18%)
Four traits	28 (8.1%)
Asymptomatic	
yes	217 (62.9%)
no	128 (37.1%)
Dyspepsia	
yes	97 (28.1%)
no	248 (71.9%)
BMI by category	
normal weight	45 (13%)
overweight	72 (20.9%)
grade I	166 (48.1%)
grade II	59 (17.1%)
morbidly obese	3 (0.9%)
Right Hypochondrial Pain	
yes	17 (4.9%)
no	328 (95.1%)
Fatigue	
yes	124 (35.9%)
no	221 (64.1%)
Hepatomegaly	
yes	66 (19.1%)
no	279 (80.9%)

The body mass index (BMI) was significantly higher in female patients as compared to males (p<0.001). The males had a significantly greater frequency of traits for metabolic syndrome as compared to women i.e. 111 (86.7%) vs. 145 (66.8%) (p=0.02). Obesity in patients was also significantly associated with female gender (Table 2).

Table 2. Gender-wise distribution of Clinical Parameters in Patients with NAFLD

Clinical Parameters	Female (217)	Male (128)	p-Value
Cholesterol mg/dl	199.5	193.9	0.543
Body Mass Index (BMI)	31.4	27.8	0.001
Diabetes Mellitus Type 2			0.118
yes	86 (39.6%)	31 (24.2%)	
no	131 (60.4%)	97 (75.8%)	
Metabolic syndrome			0.029
<2	72 (33.2%)	17 (13.3%)	
3 or greater	145 (66.8%)	111 (86.7%)	
Hypertriglyceridemia			0.119
yes	117 (53.9%)	48 (37.5%)	
no	100 (46.1%)	80 (62.5%)	
Hypercholestrolemic			0.449
yes	55 (25.3%)	41 (32%)	
no	162 (74.7%)	87 (68%)	
Obesity			0.001
yes	169 (77.9%)	59 (46.1%)	
no	48 (22.1%)	69 (53.9%)	

Upon evaluating the association of diabetes mellitus type 2 (DMT2) with clinical parameters, we found a significant relationship of hypercholesterolemia in patients with DMT2 (p=0.04). Similarly, the majority of the patients i.e. 55 (47%) with DMT2 also had hypertriglyceridemia (p=0.002) (Table 3).

Table 3. Diabetes Mellitus and its Association with Clinical Parameters in Patients with NAFLD

Clinical Parameters	Diabetes Mellitus	No Diabetes Mellitus	p-Value
Hypercholestrolemic			0.048
yes	72 (61.5%)	93 (40.8%)	
no	45 (38.5%)	135 (59.2%)	
Hypertriglyceride			0.002

mia			
yes	55 (47%)	41 (18%)	
no	62 (53%)	187 (82%)	

Patients who were overweight had significant associations with Hypercholesterolemia, Hypertriglyceridemia, and metabolic syndrome with p=0.03, 0.002, and 0.029, respectively (Table 4).

Table 4. Obesity and its Association with Clinical Parameters in Patients with NAFLD

Clinical Parameters	Overweight	Normal Weight	p-Value
Hypercholesterolemia			0.03
yes	79 (34.6%)	17 (14.5%)	
no	149 (65.4%)	100 (85.5%)	
Hypertriglyceridemia			0.002
yes	135 (59.2%)	31 (26.5%)	
no	93 (40.8%)	86 (73.5%)	
Metabolic syndrome			0.029
yes	84 (36.8%)	7 (6%)	
no	144 (63.2%)	110 (94%)	

DISCUSSION

Nonalcoholic fatty liver disease is the most widely recognised reason for raised liver enzymes and of cryptogenic cirrhosis.[7] Jimba et al, with the help of liver ultrasonography, demonstrated that NAFLD is reported to be present in 29% of the healthy Japanese adults, showing that NAFLD might be close to reaching epidemic extents.[8] Early acknowledgement of these risk factors with satisfactory management can decrease the extent of patients leading to cirrhosis. Our study suggested that the most frequent risk factors for steatosis were female gender, obesity, diabetes mellitus type 2, and hypertriglyceridemia. Several local and international data have suggested similar findings.[9-12] According to our data, the majority were females and overweight or obese. One study revealed that obesity was a significant risk factor associated with dyslipidemia. [12]

In the majority of the studies, a characteristic patient with NAFLD is a middle-aged woman, but some studies have reported a higher frequency of NAFLD in males than in females.[13-14] In a study conducted by Karam P et al. it was found that the age varied from 20-60 years with a mean age of around 40 years. The authors further revealed a significant association between NAFLD and metabolic syndrome. [13] These findings were in line with our study. A considerable risk factor for NAFLD is truncal obesity, even in patients with a normal body-mass index. Nevetheless, recent evidence has shown that NAFLD can develop in patients who are lean and not obese more specifically in Asian population. [15]

In our study, almost one-half of the NAFLD patients were reported to have hypertriglyceridemia and approximately thirty percent had hypercholesterolemia. Silverman et al has stated similar results in his study. These disordered lipid profiles were more frequently observed in obese patients, diabetics and females. [16] The severity of NAFLD increases with the rise in number and extent of metabolic risk factors. Jarvis et al conducted a comprehensive meta analysis to explore the correlation between NAFLD and metabolic risk factors. The study concluded that diabetes mellitus type 2, obesity, lipid abnormalities, and hypertension were significantly associated with an increased severity of liver disease. [17]

The occurrence of metabolic syndrome in patients with NAFLD imposes a greater risk of the disease progressing to severity, conferring an odds ratio (OR) of3.2 for the presence of NASH and 3.5 for advanced fibrosis.[18] A study conducted on 235 NAFLD patients in Saudi Arabia concluded that diabetes and obesity were the most prevalent determinants in the subjects. 14.9% had metabolic syndrome, and 3.8% had hypothyroidism. [19]

The findings of our study were similar to other findings reported in local and international studies.[9-15] However, our study has a few limitations. The nature of the design of our study is descriptive, which is weaker. Diagnosis of all our patients was made using ultrasound which is inferior as a diagnostic tool as compared to a liver biopsy as ultrasound only helps in detecting a fatty liver, but does not help in assessing the status of steatohepatitis, which is confirmed with the biopsy. Further studies are needed with a larger sample size to assess the prevalence of various risk factors in the NAFLD population with improved accuracy and confirmation.

CONCLUSION

The present study indicated that female gender, obesity, and diabetes mellitus were significantly associated with non-alcoholic fatty liver disease (NAFLD). Non-alcoholic fatty liver disease (NAFLD) places a significant burden on the healthcare system and is associated with poor quality of life of patients. Metabolic syndrome is another leading association that needs to be explored in further detail. Recognition of high-risk profile patients can help establish early diagnosis and hence treatment plans can be implemented at an early stage of disease.

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