NON-ALCOHOLIC FATTY LIVER DISEASE AT OUR INSTITUTE

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ABSTRACT

INTRODUCTION

A Correlation clinical observational hospital based clinical study with 50 patients were undertaken to study the Clinical Profile of incidentally detected Non Alcoholic Fatty Liver Disease. The cases for the study were selected retrospectively who were diagnosed as fatty liver by ultrasound imaging who attended the Department of General Medicine, Government General Hospital Kakinada Rangaraya Medical College. Data has been enumerated for those who fulfilled the inclusion criteria. This study was conducted between January 2013-January 2015. The study has limitations of observer variant dependent diagnostic ultrasound for inclusion in to study. A BMI of>25 kg/m^2 taken as definition for obesity for analysis.

KEYWORDS

NAFLD, C06.552.241.519, Diabetes Mellitus, C18.452.394.750, Dyslipidemias, C18.452.584.500.

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INTRODUCTION: The condition of liver lipid accumulation, resembling alcohol-induced injury but occurring in patients who do not use alcohol (or maximum 2-3 glasses/day), is called nonalcoholic fatty liver disease (NAFLD).[1] Several (often incorrectly used) synonyms for the same disease are diabetes hepatitis, fatty-liver hepatitis, alcohol-like liver disease, Laennec's disease and nonalcoholic steatohepatitis (NASH).[2] NAFLD is an increasingly recognized condition, fuelled by the increasing prevalence of obesity, and is very rapidly becoming a major health problem world-wide.[3,4] NAFLD in the early stage usually asymptomatic, but it is by itself a risk factor for hepatocellular carcinoma (HCC) and is also part of the natural (progressive) history of NASH, which can lead to cryptogenic fibrosis.[5,6]

Due to the risk of progression (Fig. 1) to more severe liver disease and consequences of its fibro-inflammatory process, NAFLD has been predicted to be the major cause of liver transplantation in 2020.[7] Nonalcoholic fatty liver disease is a chronic liver condition characterized by insulin resistance and hepatic fat accumulation, in the absence of other identifiable causes of fat accumulation, such as Alcohol abuse, Viral hepatitis, Autoimmune hepatitis, Alpha-1 antitrypsin deficiency, medications like corticosteroids and estrogens, and other conditions.

Hepatic steatosis may range from a 'benign' indolent deposition of fat to severe lipotoxicity-induced steatohepatitis with necrotic inflammation [known as nonalcoholic steatohepatitis (NASH)]. NASH is an overlooked complication of Type 2 diabetes mellitus (T2DM) if missed that may carry serious long-term consequences. NASH is frequently associated with fibrosis and patients may develop cirrhosis. The risk of hepatocellular carcinoma is also increased in patients with T2DM and NASH.

Diabetes, Dyslipidemia, Hypertension, and Cardiovascular disease (CVD) occur more frequently in individuals with NAFLD. NAFLD may also be associated with a greater risk of renal disease in patients with T2DM. Health care costs have been long suspected to be higher in NASH patients.

NAFLD is strongly associated with obesity, Type-2 diabetes mellitus and hyperlipidemia. Numerous studies show that it is hepatic component of metabolic syndrome whose central features are peripheral insulin resistance, obesity, hyperinsulinemia, hypertriglyceridemia and hypertension.

AIM AND OBJECTIVES:

1. To Delineate the Clinical Profile of Incidentally detected Non Alcoholic Fatty Liver Disease.
2. To assess clinical, biochemical profile of these patients.

MATERIAL AND METHOD: The cases for the study were selected retrospectively who were diagnosed as fatty liver by ultrasound imaging who attended the Department of General Medicine Government General Hospital Kakinada/Rangaraya Medical College. The study has been retrospective observational study, where data has been enumerated for those who fulfilled the inclusion criteria. This study was conducted during January 2013-January 2015. After obtaining written informed consent, a thorough medical history was taken and physical examination was performed for each individual, which included measurements of weight and height. BMI was calculated as a measure of obesity. After an over-night fasting, serum samples were obtained from all subjects for liver function tests (aspartate amino-transferase [AST], alanine aminotransferase [ALT], and alkaline phosphatase), serum lipid profile (total cholesterol, triglycerides, high-density lipoprotein cholesterol [HDL-C]

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and low-density lipoprotein cholesterol [LDL-C], fasting blood glucose (FBS) and serum insulin level.

Inclusion Criteria:

1. Age more than 30 years.
2. Fatty liver confirmed by ultrasound imaging in 50 patients.

Exclusion Criteria:

1. People with significant alcohol consumption (more than 20gms/day).
2. Presence of Hepatitis B or C virus infection.
3. Chronic liver diseases like, a. Auto immune hepatitis, b.Wilsons disease, c. Haemochromatosis.
4. Patients on medications producing steatosis with in past 6 months.
5. Patients on parenteral nutrition.

Criteria taken in to consideration for categorization: Overweight was defined as a body mass index (BMI) between 23 and 25 kg/m^2, and obesity as BMI equal or above 25kg/m^2. Patients with one of the criteria: LDL-C >100 mg/dl, total cholesterol >200mg/ dl, triglycerides >150 mg/dl, or HDL-C <40mg/dl in males and <50mg/dl in females were considered to have dyslipidemia. 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. All subjects who were confirmed as fatty liver were graded by abdominal ultrasonography by the radiologist. Based on ultrasonography findings, they were graded as mild, moderate, and severe diffuse increase in echogenicity as compared to that of the spleen or renal cortex. Degree of liver steatosis was graded on a five-point scale based on liver echogenicity Gr0 (absent), Gr1 (minimal), Gr2 (mild), Gr3 (moderate), Gr4 (severe).

RESULTS & OBSERVATIONS:

Study Design: A Correlation clinical observational hospital based clinical study with 50 patients was undertaken to study the Clinical Profile of Incidentally detected Non Alcoholic Fatty Liver Disease.

Out of 50 subjects, 38(76%) were male patients and 12 (24%) were females with a sex distribution ratio of 3.16:1 (Fig. 2) Age range was 30-80yrs (mean 52.58±11.85). Most patients were of 4th and 5th decade. Most common symptom was dyspepsia (54%) Hepatomegaly was found in 3 patients (6%).

Liver function tests varied in the following way. Hyperbilirubinemia (>1.2mg/dl) was present in 7 patients (14%). Elevated SGOT was seen in 19 patients (38%) Mean SGOT (u/l) 36.70±10.17. Elevated SGPT was seen in 28patients (56%) Mean SGPT (u/l) 47.68±12.42 (Fig. 4).

Normal BMI was found in 8 patients (16%). Overweight was found in 11 patients (22%). Obese BMI was found in 31 patients (62%). Mean BMI (kg/m^2) of study group is 26.52±3.62 (Fig. 3).

Using ADA criteria diabetes was found in4patients (8%) (FBG >126mg/dl). Impaired OGTT was found in 11 patients (22%) patients. Overt, diabetes was present in 8 patients (16%) (Fig. 5).

Hypertension was found in 10 patients (20%) Hyperlipidemia was found in 31 patients (62%) Metabolic syndrome was found in 20 patients (40%) Insulin resistance was found in 28 patients (56%). Triglycerides of >150 mg/dl were seen in 31 patients (62%) Low HDL was seen in 30 patients (60%). Mild fatty liver was seen in 39 patients (78%) Moderate fatty liver was seen in 10(20%). Severe fatty liver was seen in 1(0.5%).

Mean TG (mg/dl) 175.02±30.76 Mean cholesterol (mg/dl) 175.66±22.55. Mean HDL (mg/dl) 42.50±9.64. Mean LDL (mg/dl) 98.22±23.68. Mean total bilirubin (mg/dl) 0.94±0.38(fig6).

Mean FBG(mg/dl) of the study group was 101.04±19.03. Mean PLBS(mg/dl) of study group was 168.48±35.75 (fig5).

DISCUSSION: NAFLD emerged as a common liver problem worldwide and is found in up to 1/3 of general population. [8,9,10,11,12] There is little information on the true profile of patients with NAFLD in clinical practice. Most studies for diagnosis of NAFLD were based on selected subset of patients with transaminitis.[13,14,15,16,17] Although only about half of the patients with NAFLD have transaminitis and patients without transaminitis can harbor advanced disease.[18,19] Thus the profile of NAFLD in the published literature may in fact present a skewed picture. In our study, transaminases were elevated in 56% of patients with NAFLD -higher compared to other Indian studies[13,14] but lower than the western studies.[20,21] The present study showed NAFLD to be a disease of middle age with mean age of 52.58±11.85 years at presentation and a male predilection-three-fourths (76%) being male. We have reports earlier that the prevalence of NAFLD was two-folds higher among men. [9]

Mohan et al. and Pinidiyapathirage et al. have reported the preponderance of men.[10,22] However, Fernandes et al. and Haentjens et al., suggested female prepondarance especiallyin those who are at increased risk of developing NAFLD.[23,24] Spruss et al. Showed that female mice were more susceptible to NAFLD than male mice.[25] A recent Australian study suggested that sex differences in adolescents with NAFLD were related to differences in adipose distribution and adipocytokines.[26] The male predominance in our study may also be explained by social discrimination towards women and psychosocial inhibition among them in seeking medical attention for their problems. A majority were from middle socio economic status which probably reflects the overall socio economic status of the study population. In our study, the mean BMI was 26.52±3.62kg/m^2; 22% and 62% patients were overweight and obese, respectively. Similar findings were seen in most other Indian studies with a median BMI value of 26.7kg/m^2 with almost 60%–70% patients having obesity as defined by the Asia-Pacific criteria.[14,15,16] An exception to this is the Bengal study with very low BMI (22.7±3.90 kg/m^2).[13] This may be because the study was carried out in an extremely

underprivileged area; and as expected, the prevalence of NAFLD was only 8.7%. The Bengal findings cannot be applied to other populations. Our patients with NAFLD had a lower mean value of BMI as compared to the western figures (30–38kg/m^2).[20,21,27,28] Despite lower BMI, our patients had fatty liver, possibly due to characteristics of South Asian phenotype (i.e. greater propensity to IR and central obesity).[29] Only 16% of our patients had diabetes, while another 18% had only IGT. A lower prevalence of diabetes (7%–22%) was also found in other Indian studies.[10,13,14,15,16] This is in contrast to western figures-38% cases of diabetes in NAFLD (UK).[24] While among Americans, diabetes was associated with half of histologically proven patients with NAFLD.[30] In our study, the prevalence of mild steatosis was 40%; in contrast in the New Delhi study, in which mild steatosis was found in only 20% of patients.[15] This difference may be due to the higher FBG cutoff level of >110mg% for diagnosis of diabetes and the inclusion criterion of transaminitis in this study. Our study was USG-based and a more appropriate FBG cut-off level of >100mg/dl was used. The pathogenesis of NAFLD involves a two-hit hypothesis. [31] The first hit is steatosis, and the second hit leads to transformation from steatosis to steatohepatitis. Insulin resistance (IR) is believed to play an important role in both these hits. [32] In the present study, the prevalence of IR was only 56%. In contrast, other Indian studies reported a higher frequency of 80%–83%. [15,16] A lower cut-off value (IR >1.64) used in these studies may account for a higher prevalence of IR among them. In the present study, the mean serum TG and mean serum LDL levels were above the normal upper limit, while the mean serum HDL level was below the normal limit, signifying that most patients had dyslipidemia—a known risk factor for fatty liver. In summary, the present study revealed that our Government General Hospital subjects with NAFLD were younger, had lower BMI, lower prevalence of diabetes mellitus and, mild steatosis but similar necrotic inflammatory activity and fibrosis as compared to that reported in the West.

LIMITATIONS:

1. All patients were diagnosed only on the basis of USG findings whose sensitivity and specificity is observer-dependent. The difficulty in detecting the presence of fatty liver with USG is well known in morbidly obese patients, and when the degree of fat infiltration is <33% of the hepatic content.
2. Defining obesity as BMI >25kg/m^2 may not be acceptable to many physicians. This could also be true for the use of BMI as a surrogate marker for waist circumference, which may not always be true. Indian subjects may have a normal BMI but an abnormal waist which is more closely related to central obesity rather than overall obesity.
3. As the present study was clinic-based and not a cross-sectional population study, the findings of this study may not be truly representative and applicable to the general population at large.

CONCLUSION: Despite the limitations, this is a unique attempt to characterize and define the profile of patients with incidentally detected NAFLD who are commonly encountered in clinical practice and constitute the bulk of the patients with NAFLD. Our findings have important clinical and public health implications. This study also evaluated and analyzed the clinical diseases associated with NAFLD. Further, patients with NAFLD were predominantly men, most of whom were not lean. Only about half the patients had Transaminitis. Prevalence of NAFLD appears to be substantially higher than that predicted on the basis of elevated ALT levels. Male sex, BMI, transaminitis and mild steatosis were independently associated with ultrasonographic severe fatty change. Early detection, as well as steps to prevent the condition through lifestyle modification may halt the progression of a benign disease to advanced illness. It is important for physicians and general practitioners to be aware about the clinical, biochemical and histological profile of NAFLD which is such a common liver disorder.

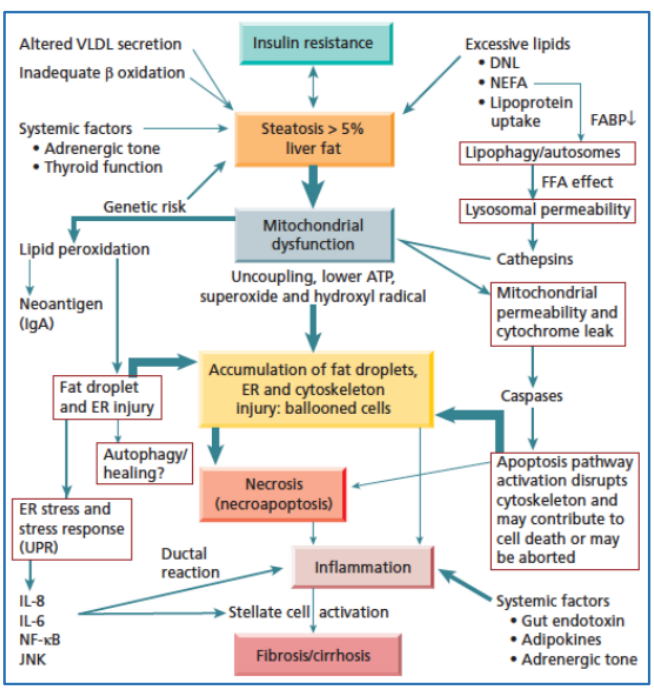

Fig. 1: Progression of NAFLD

Age in years	Number of patients	%
31-40	9	18
41-50	11	22
51-60	20	40
61-70	6	12
71-80	4	8
Total	50	100

Fig. 2: Age distribution

BMI	Number of patients	%
18.6-22.9	8	16
23-24.9	11	22
>25	31	62
Total	50	100.0

Fig. 3: BMI (kg/m²) of patients studied

Enzymes	Number of patients (n=50)	%	Mean
SGOT (IU/L)			36.70+_10.17
<42	31	62	
>42	19	38	
SGPT (IU/L)			47.68+_12.42
<33	22	44	
>33	28	56	

Fig. 4: Liver enzymes

Glucose parameters	Number of patients (n= 50)	%	Mean
FBS (mg/dl)			101.04+_19.03
• <110	37	74	
• 110-126	9	18	
• >126	4	8	
PPBS (mg/dl)			168.48+_35.75
• <140	33	66	
• 140-200	11	22	
• >200	6	12	

Fig. 5: Glycemic Indices

Lipid parameters	Number of patients (n=50)	%	Mean
Total cholesterol mg/dl			175.66+_22.55
• <200	39	78	
• >200	11	22	
Triglycerides (mg/dl)			175.02+_30.76
• <150	19	38	
• >150	31	62	
HDL (mg/dl)			42.50+_9.64
• <40	30	60	
• >40	20	40	
LDL (mg/dl)			98.22+_23.68
• <100	25	50	
• >100	25	50	

Fig. 6: Lipid parameters of patients studied

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