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ORIGINAL RESEARCH

Clinical & histological profile of patients with nonalcoholic fatty liver disease

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ABSTRACT

Background: The estimated prevalence of fatty liver in the general population averages around 14-25 % with rising prevalence in the presence of risk factors. Liver biopsy continues to be the ultimate and specific investigation for assessing the nature and severity of a spectrum of liver diseases. Present study was aimed to study clinical & histological profile of patients with nonalcoholic fatty liver disease.

Material and Methods: This study was retrospective and prospective, observational study, conducted in patients with increased echo texture of liver on routine ultra-sound scan, suggestive of fatty liver disease, prior to performing percutaneous liver biopsy, the proper preparation of a patient is important, with attention to a detailed knowledge of the procedure, a complete history and physical evaluation, medication use, and fresh clotting parameters.

Results: In present study, among 60 patients, 36 (60%) were females and 24(40%) were males. Majority were from the age group of 41- 50 years (36.66%), followed by 51-60 years (30 %). Commonest symptom was fatigability and malaise (66.66%), followed by right upper abdominal discomfort (46.66%), Jaundice (10%), ascites (10%), UGI Bleed (8.3%) patients and 20 (33.33%) patients were asymptomatic at the time of diagnosis. The commonest clinical sign was of hepatomegaly or palpable liver (90%), edema (35 %), abdominal distension (18.33 %), splenomegaly (16.67 %) & icterus (13.33 %). Various risk factors noted were dyslipidemia (61.67 %), diabetes mellites (58.33 %), hypertension (53.33 %), overweight (50 %), obese (46.67 %) & coronary artery disease (40 %). 7 patients underwent biopsy. Of these 4.28% patient showed steatohepatitis, 42.86% patients showed simple fatty change and 14.28% patient had cirrhosis. Other 28.57% had no specific changes.

Conclusion: Our findings were consistent with the earlier concept that non-alcoholic steatohepatitis was prevalent in obese females with diabetes and hyperlipidemia.

Keywords: Liver biopsy, non-alcoholic steatohepatitis, diabetes, hyperlipidemia

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INTRODUCTION

The estimated prevalence of fatty liver in the general population averages around 14-25 % with rising prevalence in the presence of risk factors.[1] In western countries most cases are attributable to alcohol excess, however, it may also occur in association with a wide range of toxins, drugs and diseases, such as other primary hepatic disorders, morbid obesity, type 2 diabetes, hyperlipidemia, after jejunoileal bypass surgery and debilitating diseases with cachexia.[1,2]

Fatty liver disease can etiologically be divided into two major categories: Alcoholic fatty liver disease (AFLD) and non-alcoholic fatty liver disease (NAFLD). Alcoholic fatty liver disease and the effect of alcohol on mortality has been well characterized in many studies, while nonalcoholic fatty liver disease is a relatively new disease and was not described until 1980, when Ludwig published a paper characterizing this alcohol-like disease in non-alcoholic patients.[3]

Liver biopsy continues to be the ultimate and specific investigation for assessing the nature and severity of a spectrum of liver diseases. Patients with nonalcoholic fatty liver, including non-alcoholic steatohepatitis, with fibrosis is in liver biopsy had more liver related deaths than patients without fibrosis, clinical, biochemical or imaging studies, although useful in the detection of hepatic steatosis, are not sensitive enough to detect the degree of hepatic fibrosis.[4,5] Present study was aimed to study clinical & histological profile of patients with nonalcoholic fatty liver disease.

MATERIAL AND METHODS

This study was retrospective and prospective, observational study, conducted in department of general medicine, at Kamineni Institute of Medical College Hospital, Narketpally, India. Study was conducted during period of September 2019 to October 2021 (2 years). This study was reviewed and approved by the institutional ethical committee.

Patients with increased echo texture of liver on routine ultra-sound scan, suggestive of fatty liver disease, willing to participate in this study were considered for present study. Alcoholic patients, patients with viral hepatitis (B and/or C), sepsis, total parenteral nutrition, jejuno-Ileal by-pass, Auto-immune disease, had rapid weight loss, on drugs (steroids, tamoxifen, hormone replacement therapy, nifedipine, diltiazem, methotrexate, amiodarone, warfarin, pentoxifylline, chloroquine) were not considered for presents study.

Study was explained to patients in local language & written consent was taken for participation & study. All cases included into the study underwent a complete clinical, anthropometric and laboratory evaluation after a screening ultra-sound scan of liver. Brightness and posterior attenuation were considered indices of the extent of fatty infiltration and fibrosis and were graded appropriately by a single radiologist.

Elisa technique was used for all the serological investigations which include HIV, HbSAg, HCV, ANF, Serum Insulin and other antibodies. Clotting parameters (Prothrombin time, partial thromboplastin time, a complete blood count with platelet count, and a bleeding time) were done on day of evaluation. Complete blood counts (Hemoglobin, Total Leukocyte counts and Differential leukocyte counts and Platelets) were measured with automatic instrument. TLC and DLC were confirmed with manual counting also. Erythrocyte Sedimentation Rate (ESR) was measured with Wintrobe's Tube in the first hour. Serum Urea,

Creatinine, Total Serum Proteins, Albumin, Bilirubin, Transaminases, Alkaline phosphatase, Lipid profile was done.

Prior to performing percutaneous liver biopsy, the proper preparation of a patient is important, with attention to a detailed knowledge of the procedure, a complete history and physical evaluation, medication use, and fresh clotting parameters A thorough written consent that has detailed explanation of the major complications was taken. Transcutaneous liver biopsy was done as per standard operating procedures, with local anaesthesia by automated liver biopsy gun (BARD) under ultrasound guidance. Automated liver biopsy gun position in the liver tissue was confirmed by the movement with respiration and then the lock was released and the needle was removed. This completed the tissue collection and the tissue so obtained was placed in 10% formalin and sent to the laboratory for further processing. After the procedure the patient was placed in the right lateral position for a few hours and adequate analgesia was given and observed for 24 hours.

All data was compiled in Microsoft access and excel database. Statistical analysis was done using descriptive statistics.

RESULTS

In present study, among 60 patients, 36 (60%) were females and 24(40%) were males. Majority were from the age group of 41- 50 years (36.66%), followed by 51-60 years (30 %).

Table 1: General characteristics

	No. of patients	**Percentage**
Age groups (in years)		
21-30	2	3.33%
31-40	9	15.00%
41-50	22	36.67%
51-60	18	30.00%
61-70	9	15.00%
Mean age (mean ± SD)	50.86 ± 9.27 years	
Gender		
Male	24	40.00%
Female	36	60.00%

In present study, commonest symptom was fatigability and malaise (66.66%), followed by right upper abdominal discomfort (46.66%), Jaundice (10%), ascites (10%), UGI Bleed (8.3%) patients and 20 (33.33%) patients were asymptomatic at the time of diagnosis. The commonest clinical sign was of hepatomegaly or palpable liver (90%), edema (35 %), abdominal distension (18.33 %), splenomegaly (16.67 %) & icterus (13.33 %).

Table 2: Clinical features

Characteristic	**No. of patients**	**Percentage**
Fatigability	40	66.67%
Malaise	40	66.67%
Right upper abdominal discomfort	28	46.67%
Jaundice	6	10.00%
Ascites	6	10.00%
UGI Bleed	4	6.67%
Asymptomatic	20	33.33%
Signs		
hepatomegaly or palpable liver	54	90.00%
Edema	21	35.00%

Abdominal distension	11	18.33%
Splenomegaly	10	16.67%
Icterus	8	13.33%

Various risk factors noted were dyslipidemia (61.67 %), diabetes mellites (58.33 %), hypertension (53.33 %), overweight (50 %), obese (46.67 %) & coronary artery disease (40 %).

Table 3: Risk factors

Risk factors	No. of patients	Percentage
Dyslipidemia	37	61.67%
Diabetes Mellites	35	58.33%
Hypertension	32	53.33%
Overweight	30	50.00%
Obese	28	46.67%
Coronary Artery Disease	24	40.00%

All patients were negative for HIV, HbSAg, HCV and other markers of autoimmune hepatitis (ANA, AMA, etc.). Among, RFT's mean blood urea level were 27.10 ± 27.66 mg/dl & mean serum creatinine level was 1.89±1.01 mg/dl. The mean prothrombin time (FT) was 14.18 ± 2.28 sec and mean partial thromboplastin time was (APTT) was 34.11 ±6.89 seconds.

Mean total serum proteins was 6.56 ± 0.75 gm/dl, mean serum albumin was 1.9 - 5.2 gm/dl, mean total bilirubin was 1.17 ± 1.03 mg/dl, mean conjugated fraction was 0.21 ± 0.44 mg/dl, mean alkaline phosphatase was 234.78 ± 115.30 IU/L, mean serum glutamate pyruvate transferase (SGPT) was 57.47 ± 51.39 IU/L and mean serum glutamate oxaloacetate transferase (SGOT) was 46.88 ± 31.95 IU/L.

The mean total cholesterol level was 187.43 ± 91.88 mgm/dl, mean HDL cholesterol level was 34.9 ± 12.79 mgm/dl, mean LDL cholesterol level was 112.53 ± 39.31 mgm/dl, mean VLDL cholesterol level was 41.92 ± 37.30 mgm/dl, mean triglyceride level was 205.96 ± 109.25 mgm/dl.

Table 4: RFT, LFT, clotting function & serum lipids

Characteristic	Mean ± SD	Range
Renal function tests		
Blood urea	27.10 ± 27.66 mg/dl	11-214 mg/dl
Serum creatinine	1.89 ± 1.01 mg/dl.	0.6-6.7 mg/dl
Clotting Parameters		
Prothrombin time (PT)	14.18 ± 2.28 sec	10-20 seconds
Partial thromboplastin time (APTT)	34.11 ± 6.89 sec	20 - 60 seconds.
Liver function tests		
total serum proteins	6.56 ± 0.75 gm/dl.	5 - 8.2 gm/dl
Serum albumin	3.63 ± 0.71 gm/dl.	1.9 - 5.2 gm/dl
Total bilirubin	1.17 ± 1.03 mg/dl.	0.3-5.4 mg/dl
Conjugated	0.21 ± 0.44 mg/dl.	0 - 1.6 mg/dl
Alkaline phosphatase	234.78 ± 115.3 IU/L.	115 - 653 IU/L
Serum glutamate pyruvate transferase (SGPT)	57.4 ± 51.39 IU/L	11- 263 1U/1
Serum glutamate oxaloacetate transferase (SGOT)	46.8 ± 31.95 IU/L	13-200 IU/1.
Serum Lipid		
Total cholesterol	187.43 ± 91.88 mgm/dl	94 -819 mgm/dl.

HDL	34.9 ± 12.79 mgm/dl	7-62 mgm/dl.
LDL	112.5 ± 39.31 mgm/dl	30 - 300 mgm/dl.
VLDL	41.92 ± 37.30 mgm/dl	3-230 mgm/dl.
Triglyceride level	205.9 ± 109.2 mgm/dl	46-652

7 patients underwent biopsy. Of these 4.28% patient showed steatohepatitis, 42.86% patients showed simple fatty change and 14.28% patient had cirrhosis. Other 28.57% had no specific changes. Of these 2 patients one had glycogen deposits in the hepatocytes and the other patient had a normal liver biopsy.

Table 5: Liver biopsy

Liver Biopsy	Frequency (N=7)	Percentage
Steatohepatitis	1	14.29%
Cirrhosis	2	28.57%
Simple fatty change	4	57.14%
• No specific changes	2	28.57%
• Normal liver biopsy	2	28.57%

DISCUSSION

Non-alcoholic fatty liver disease/ steatohepatitis (NASH) affects the large portion of the world's population. Non-alcoholic steatohepatitis is an increasingly recognized chronic liver disease because of its potential to progress to end stage liver disease. The pathological features resemble that of alcohol-induced liver injure, but it occurs in patients who do not abuse alcohol.

Non-alcoholic steatohepatitis was considered to be a medical curiosity for many years but now it is a well-established cause of chronic liver disease in the western world. There is dearth of literature about the magnitude of non-alcoholic steatohepatitis in Indian subcontinent. The available reports (Aggarwal et al.,[2] Gupte et al.,[6]) confirms that non-alcoholic steatohepatitis equally prevalent in Indian population. This emerging disease must be tackled at many levels and from many directions to limit the morbidity and mortality associated with non alcoholic steatohepatitis.

Majority of our patients 36 (60%) were females and this high female prevalence in our study was similar to the study of Aggarwal et al.,[2] and may have several potential explanations. They may either reflect social attitude patterns in the local population or alternatively they may reflect referral bias.

In present study, common symptoms were fatigability and malaise (66.66 % each), followed by right upper abdominal discomfort (46.66%). These findings were contrary to the findings of Lee JG[8] & Agarwal et al. 2001.[2] The predominant population studied was females who might be having associated nutritional anaemia which is a common coexisting problem in many females in India, which was not analysed further.

The commonest clinical sign detected in this study was of hepatomegaly or palpable liver found in 54 (90%) subjects. This disease commonly progresses without much clinical symptoms and signs. Similar findings were noted by Angulo et al.,[5] In present study, obesity, hyperlipidemia and diabetes mellitus are the most commonly associated risk factors for the development of fatty liver disease. These findings were similar to the findings from Agarwal et al.,[2] and Marchesini G et al.,[9]

The mean serum glutamate oxaloacetate transferase (SGOT) was 46.88±31.95 IU/L and ranged from 13 -200 IU/1. 31 (51.67%) had SGOT elevation more than 40 IU/L and 37 (61.67%) had SGPT elevation more than 40 IU/L. These findings were similar to the findings of Dhiman RK et al.,[9] and Pinto F et al.,[10] where the most common abnormality in liver Function test was two-to-five-fold elevation of transaminases.

As evident from the study of Pinto TK et al.[11] serum alkaline phosphatase were above the normal range in many patients. In this study also 25 (41.67%) patients had level of alkaline phosphatase above normal. Alkaline phosphatase levels ranged from 115 - 653 IU/L and the mean was 234.78±115.30 IU/L. Similar findings were noted by Mathieson NL et al.,[12]

The histological spectrum of fatty liver disease ranges from simple steatosis to steatohepatitis, fibrosis and ultimately cirrhosis. Fatty liver is characterized by the cumulation of lipid within the cytoplasm of hepatocytes and is a common finding in human-liver biopsy specimens. [1,3]

Two major patterns of fatty liver are recognized: macrovesicular and microvesicular, though often seen in a mixed pattern. Features of liver cell injury and associated necroinflammation may accompany steatosis. This constellation of findings is referred to as steatohepatitis. Liver fibrosis may develop progressively, and end-stage of liver fibrosis is cirrhosis, which is a diffuse process characterized by bridging fibrosis and conversion of the normal liver architecture into structurally abnormal nodules.[13,14,15]

Diagnosis of non-alcoholic fatty liver disease can be established by a liver biopsy. Among 7 patients underwent biopsy. Of these 1(14.28%) patient showed steatohepatitis, 3 (42.86%) patients showed simple fatty change and 1 (14.28%) patient had cirrhosis. Other 2 (28.57%) had no specific changes. Of these 2 patients one had glycogen deposits in the hepatocytes and the other patient had a normal liver biopsy.

This study had some limitations namely financial and paucity of liver biopsies. Serum Insulin levels could not be done all the patients for comparing insulin resistance for both diabetics and non-diabetics since it was a costly investigation. Consent for liver biopsy was also very difficult since most of these patients were asymptomatic at presentation. Follow up of these patients over a period of time was also difficult since this would have helped in assessing the improvement and response to different treatment modalities used i.e. Urso deoxycholic acid, Vit E, etc.

CONCLUSION

Liver biopsy remains the best diagnostic tool for confirming non-alcoholic steatohepatitis. Our findings were consistent with the earlier concept that non-alcoholic steatohepatitis was prevalent in obese females with diabetes and hyperlipidemia. Our observations have corroborated the other reports of non-alcoholic steatohepatitis in Indians population that non-alcoholic steatohepatitis is often seen in men in the absence of diabetes and hyperlipidemia.

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